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A TEXT-BOOK OF
HUMAN PHYSIOLOGY

A TEXT-BOOK OF
HUMAN PHYSIOLOGY

BY

DR. ROBERT TIGERSTEDT
PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF HELSINGFORS, FINLAND

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TRANSLATED FROM THE THIRD GERMAN EDITION
AND EDITED BY
JOHN R. MURLIN, A.M., PH.D.
ASSISTANT PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE, NEW YORK CITY

WITH AN INTRODUCTION TO THE ENGLISH EDITION
BY
PROFESSOR GRAHAM LUSK, PH.D., F.R.S. (EDINB.)

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PREFACE TO THE FIRST EDITION

To set fixed limits to the subject matter of physiology is a very difficult task, because, properly conceived, large portions of the entire group of medical and biological sciences belong to its province. A text-book designed primarily for medical students can, however, regard the field as somewhat more restricted; for the prospective physician has abundant opportunity to amplify his knowledge of the bodily functions from his other studies. Hence in this book I have followed the usual custom and have brought together only so much of our information respecting the human body as can be described as pertaining to its normal functions. The discoveries made in the realms of practical medicine, of experimental pathology and of pharmacology, which in many respects are so full of significance for the processes of the body, are, therefore, for the most part passed by. In like manner the facts of comparative physiology have been alluded to only in exceptional cases, since an exhaustive discussion of them would have increased the size of the book to a not inconsiderable extent.

For the same reason I have been unable to find a place for the short histological discussion customary in text-books. I do not regard this as an error, for a necessarily brief and superficial résumé of the most important histological facts could be of no great service, since the student needs a more extensive knowledge of the finer structure of the body and must in any case obtain this from the text-books devoted especially to that subject. I do not therefore at all mistake the great importance of histology for physiology; on the contrary, I would recommend that in the study of a text-book of this science a text-book of histology (and one of anatomy) be always at hand in order to combine the physiological facts with the histological and anatomical facts.

Physiological chemistry also has developed so far that more and more it can claim the right to be regarded as an independent science. On the other hand it is not possible to present the physiological facts without reference to the chemical processes of the body. While therefore I am compelled to touch upon the facts of physiological chemistry, I have limited the discussion to the most important facts of all, leaving matters of detail and controverted questions to the text-books of physiological chemistry. In preparing these sections of the book I have received very valuable advice from my distinguished friend Herr Professor Dr. K. A. H. Mörner.

I may say further that the discussion of the chemical processes of the body is based in the main upon the text-books of Hammarsten and Neumeister. The experienced reader will find also that I have made frequent use of the physiological monographs which have appeared within recent years. Especially to be mentioned are the "Allgemeine Physiologie" of Verworn and "Die Zelle und die Gewebe" of O. Hertwig, which constitute the chief sources of the chapter on the cell.

With regard to the physiology of the sense organs I may state that I have treated them in this book chiefly from the point of view of the practicing physician. For this reason the physical conditions of sensation have been discussed rather fully, while those investigations on sense perception falling within the borderland common to physiology and psychology, and of themselves so extremely important, have been discussed only in roughest outline, an exhaustive discussion being quite beyond the scope of the book.

In the citation of authorities I have tried to hold a middle course between the very numerous references found in many text-books and the entire absence of them found in others. I must acknowledge, however, that I have not in all cases succeeded in finding the proper middle course.

The few references given will direct the reader's attention to only the more recent monographic discussions of the appropriate sections. Probably I should have referred throughout to the "Handbuch der Physiologie" edited by Hermann. I must content myself, however, with citing it here once for all.

Among the many beautiful illustrations, which I owe to the liberality of my publisher, the majority have been taken from the original papers of the authors cited in the figures. Figs. 3, 6, 7, 55, 61, 80, 83, 86, 87, 88, 121 have been borrowed, with the courtesy of the publishers, from "Physiologischen Graphik" of Langendorff.

ROBERT TIGERSTEDT.

STOCKHOLM, May 1, 1897.

PREFACE TO THE THIRD EDITION

WHILE adhering to the same principles which I have followed in previous editions of this book, I have in the present edition thoroughly revised almost all the chapters. In this work of revision the monographic discussions contained in the "Ergebnissen der Physiologie" have been of very great service to me, and I would especially direct the reader who may be interested in a deeper study of modern physiology to this collective work.

The more recent literature bearing on the subjects contained in Chapters I to XIV inclusive could for the most part be brought up only to the end of 1903. In the revision of the remaining chapters I have been able to make use of the literature of the first half of the present year.

ROBERT TIGERSTEDT.

HELSINGFORS, October 1, 1904.

TRANSLATOR'S PREFACE

In preparing this abridged edition of Professor Tigerstedt's well-known "Lehrbuch der Physiologie des Menschens" it has been my endeavor to bring the book within the reach of the second-year medical student in this country. Believing that those who would make use of the more highly technical parts of the book, as, for example, the mathematical considerations affecting the dynamics of the circulation and the optics of vision, already have access to these very valuable discussions in the German, I have, with the author's permission, omitted these parts. All other omissions and condensations have been made with the single idea already named. I shall not here enumerate these changes, because, with the exception of a very few minor ones, which in the interest of clearness it has seemed necessary to make in the proofs, all abridgments have received the author's expressed approval. Professor Tigerstedt has placed me under very great obligations for the readiness he has shown both to adopt my suggestions and to make others of his own motion.

In the actual work of translation I have labored throughout to give the author's thought a clear and accurate expression. While feeling my obligations to the author, therefore, I have endeavored (not always with success) to leave as little resistance to the thought in the form of German idiom and construction as possible.

Following in general the author's usage, I have employed italics for three purposes: for generic and specific names, for emphasis, and for indicating the key word, phrase, or clause of a paragraph. In this latter use they serve the purpose of subordinate headings.

The few additions to the text which I have ventured to make and for which I assume entire responsibility, have been selected from the most recent literature and will be found, either enclosed in brackets or in the form of foot-notes, bearing the customary signature.

After examining a number of the additional illustrations which I proposed be introduced for the benefit of American students, Professor Tigerstedt gave me his entire authorization to make such additions as I might deem suitable. The authors from whose works these illustrations were originally taken are indicated in the several legends which accompany them and

the immediate sources from which I have obtained them are mentioned in the List of Illustrations.

Finally, I wish to express my sincere thanks to Professor Graham Lusk for many suggestions by which I have profited in my editorial capacity, and to Professor Percy M. Dawson of the Johns Hopkins Medical School for reading the entire proof.

J. R. M.

New York, 1906.

INTRODUCTION TO THE AMERICAN EDITION

"TIGERSTEDT's Physiology" has been the standard text-book of German students ever since its first publication in 1897. The preparation of a third German edition afforded an opportunity of translating the work into English as the new proof was delivered from the foreign presses. Dr. Murlin presents the result of this task in the following careful and accurate reproduction of the original.

The biological introduction is an admirable chapter of the book, affording as it does a broad insight into the processes of the humbler forms of living things. In view of the large participation in this department of physiology by workers in our own country, this feature of the book will be especially welcomed.

Tigerstedt early wrote a monograph on the circulation of the blood which to-day stands unrivaled, and in this important section of physiology the present text-book is of commanding authority. He later established a respiration apparatus for experiments on the metabolism of men, and this he used not only in health but also for determinations of the life processes in diseased conditions. Tigerstedt is the only author of a general text-book of physiology who has had any experimental knowledge in this branch of science. His chapter on metabolism is the most complete general account given in any text-book in any language, and it is certain to have a wide influence among the many in this country who are striving to obtain a knowledge of those inner processes of the body which determine dietary requirements in health as well as in disease.

The treatment of the subject of the central nervous system, and the generalizations regarding its functions, is a masterpiece of its kind. In the other parts of the book a wide range of knowledge is presented with a sustained excellence of arrangement, and with that catholicity of selection which has made the book so successful in other lands.

It has been said that good physiology is the best preventive of bad medicine. Tigerstedt's physiology is essentially good physiology, presenting a picture of the modern scientific structure upon which modern medical practice is based. It must be granted that some of the phenomena of life are to be explained only by theoretical induction. But this is the daily experience of every physician as regards his patient, for he is called upon to interpret disease caused by processes which he cannot see. Tigerstedt's judicious selection of the facts of physiology, and their interpretation along lines of modern critical research, afford to the student of medicine an opportunity for that kind of intellectual training which best fits him to interpret phenomena both of health and of disease.

The book may be earnestly commended to the medical student and to the practitioner.

GRAHAM LUSK.

UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE,
NEW YORK.

TABLE OF CONTENTS

PAGE
INTRODUCTION . . . 1
CHAPTER I.—General Physiological Method . . . 4
§ 1. Physical, Chemical, and Histological Methods . . . 4
§ 2. Experiments on Living Animals . . . 5
§ 3. Experiments on Surviving Organs . . . 6
§ 4. The Graphic Method . . . 6
A. The Kymograph . . . 7
B. Time Recorders . . . 10
C. Recording by Air-transmission . . . 11
D. Registration by Photography . . . 13
CHAPTER II.—The Cell . . . 15
§ 1. General Considerations . . . 15
A. The Cell as an Elementary Organism . . . 15
B. The Reciprocal Relations between the Nucleus and Protoplasm . . . 17
C. Physical and Chemical Properties of Protoplasm . . . 19
D. Morphology of the Cell Contents . . . 20
§ 2. The Vital Phenomena of Cells . . . 22
A. Introductory Survey . . . 22
B. The Ingestion of Food . . . 30
C. Digestion . . . 38
D. The Oxidative Processes . . . 39
E. Elimination of Decomposition Products . . . 40
F. Secretion . . . 41
G. Motility . . . 42
H. Production of Light . . . 45
I. Formation of Heat . . . 46
J. Generation of Electricity . . . 46
§ 3. The Effect of External Influences on Cells . . . 50
A. On Stimuli in General . . . 50
B. Automatic Excitation . . . 52
C. Chemical Stimulation . . . 52
D. Mechanical Stimulation . . . 56
E. Stimulation by Means of Light . . . 56
F. Stimulation by Means of Heat . . . 58
G. Electrical Stimulation . . . 59
H. Cosmic Influences . . . 61
I. Conductivity . . . 62
J. The Assimilative Processes Induced by Stimulation . . . 62
K. Paralysis and Fatigue . . . 65
§ 4. Death . . . 66

PAGE
CHAPTER III.—The Chemical Constituents of the Body . . . 68
§ 1. The Nitrogenous Substances . . . 68
A. The Simple Proteids . . . 68
B. The Compound Proteids . . . 75
C. Substances Resembling Proteids . . . 77
D. Other Nitrogenous Substances . . . 78
§ 2. The Nonnitrogenous Substances . . . 79
A. Fats . . . 79
B. Cholesterin . . . 80
C. Carbohydrates . . . 80

CHAPTER IV.—Metabolism and Nutrition . . . 83
First Section: Metabolism . . . 83
§ 1. On the Method of Metabolism Experiments . . . 83
A. The Ingesta . . . 83
B. Determination of the Excreta . . . 84
C. Apportionment of the Individual Elements to the Different Excreta . 89
D. Example of a Metabolism Experiment . . . 91
§ 2. Potential Energy of the Foodstuffs . . . 92
§ 3. Metabolism in Fasting . . . 95
A. The General Condition in Fasting . . . 95
B. Character of the Metabolism in Fasting . . . 96
C. Loss of Substance from the Different Organs . . . 97
§ 4. Influence of Food on the Metabolism . . . 98
A. Influence of the Quantity of Proteid in the Food on Proteid Metabolism 99
B. The Total Metabolism after Ingestion of Proteid . . . 102
C. Metabolism after Ingestion of Fat . . . 104
D. Metabolism after Ingestion of Carbohydrates . . . 105
E. Summary and Discussion . . . 107
F. Metabolism after Ingestion of Albumoses, Fatty Acids, Gelatin, Alcohol, etc. . . . 108
§ 5. Influence of Muscular Work on Metabolism . . . 110
§ 6. Influence of the Surrounding Temperature on Metabolism . . . 114
§ 7. Metabolism in Animals of Different Size . . . 117
§ 8. Retention of Proteid in the Body . . . 120
§ 9. Storage of Carbohydrates in the Body . . . 124
§ 10. Storage of Fat in the Body . . . 129
§ 11. The Inorganic Foodstuffs . . . 131
A. General . . . 131
B. Phosphorus . . . 132
C. Calcium and Magnesium . . . 133
§ 12. Flavors . . . 133
§ 13. On the Theory of Metabolism . . . 134

Second Section: Nutrition of Man . . . 137
§ 1. Utilization of Foodstuffs . . . 138
A. Proteid . . . 137
B. Fat and Carbohydrates . . . 137
C. Mixed Diet . . . 138
§ 2. The Energy Requirements of an Adult . . . 140
§ 3. Nutrition of the Young . . . 143
§ 4. Construction of the Diet from the Different Articles of Food . . . 145

PAGE
CHAPTER V.—The Blood 147
§ 1. The Amount of Blood in the Body 148
§ 2. The Formed Constituents of the Blood 148
A. The Red Blood Corpuscles 148
B. The White Corpuscles 153
C. The Blood Platelets 153
§ 3. The Plasma 154
A. Chemical Constitution of the Plasma 154
B. Coagulation of Blood 157

CHAPTER VI.—Circulation of the Blood 161
First Section: General Survey of the Blood's Movements 161
Second Section: The Movements of the Heart 162
§ 1. The Form Changes of the Heart in Systole 162
A. Structure of the Ventricular Wall 162
B. The Form Changes of the Heart 163
§ 2. Regulation of the Blood Flow through the Heart 165
A. The Atrio-ventricular Valves 165
B. The Semilunar Valves 167
§ 3. The Heart Sounds 167
§ 4. Pressure Changes in the Heart During Its Activity 168
A. Technique 168
B. Pressure Variations in Different Chambers of the Heart 169
§ 5. The Apex Beat 172
§ 6. Time Relations of the Cardiac Events 176
§ 7. Filling of the Heart in Diastole 176
§ 8. Power and Work of the Heart 177
A. Power 177
B. Work 178
§ 9. Properties of Heart Muscle 179
A. The Nature of the Cardiac Contraction 179
B. Nutrition of the Heart 180
C. The Behavior of Heart Muscle under Direct Stimulation 182
§ 10. The Cause of the Rhythmical Activity of the Heart 185
§ 11. The Efferent Cardiac Nerves 188
A. The Inhibitory Nerves 188
B. The Accelerator Nerves 191
§ 12. The Heart Reflexes 193
§ 13. The Cardiac Nerve Centers 195
§ 14. Rate of the Heart Beat 196
Third Section: The Blood Flow 198
§ 1. The Flow of a Liquid in Rigid Tubes 198
§ 2. The Flow of a Liquid in Elastic Tubes 199
§ 3. The Flow of Blood in the Arteries 200
A. Elasticity of Arterial Wall 200
B. Methods for the Determination of Blood Pressure 202
C. Height of the Blood Pressure 204
D. Velocity of the Blood in the Arteries 209
§ 4. The Arterial Pulse 212
A. The Movement of Waves in Elastic Tubes 212
B. The Pulse 214
§ 5. Final Survey of the Movements of the Blood in the Arteries 218

PAGE
§ 6. The Flow of Blood in the Capillaries . . . 219
§ 7. The Flow of Blood in the Veins . . . 223
  A. Pressure and Velocity . . . 223
  B. Aids to the Blood Flow in the Veins . . . 224
§ 8. The Lesser Circulation and the Respiratory Variations of Blood Pressure 227
  A. The Pulmonary Circulation . . . 227
  B. Respiratory Variations of Blood Pressure . . . 229
§ 9. Vasoconstrictor Nerves . . . 231
§ 10. Vasodilator Nerves . . . 234
§ 11. Vasomotor Reflexes . . . 235
§ 12. The Vasomotor Centers . . . 237
§ 13. General Considerations on the Distribution of Blood in the Body . . . 239
  A. Mechanical Influences . . . 239
  B. The Influence of Vasomotor Nerves . . . 240

CHAPTER VII.—Digestion . . . 242
First Section: The Digestive Fluids . . . 242
§ 1. General Survey . . . 242
§ 2. Saliva . . . 245
§ 3. Gastric Juice . . . 246
  A. The Acid of the Gastric Juice . . . 247
  B. Pepsin . . . 248
  C. Rennin . . . 250
  D. Gastric Steapsin . . . 250
§ 4. Pancreatic Juice . . . 251
  A. The Amylolytic Enzymes . . . 251
  B. The Proteolytic Enzyme, Trypsin . . . 252
  C. Lipolytic Enzyme, Steapsin . . . 253
§ 5. Bile . . . 253
§ 6. Intestinal Juice . . . 255
Second Section: Secretion of the Digestive Fluids . . . 256
§ 1. General Survey . . . 256
§ 2. The Salivary Glands . . . 257
  A. Secretory Nerves . . . 257
  B. Morphological Changes During Secretion . . . 261
§ 3. The Glands of the Stomach . . . 263
  A. Secretory Nerves . . . 263
  B. The Gastric Glands . . . 266
  C. Why Does the Stomach not Digest Itself? . . . 269
§ 4. Secretion of Pancreatic Juice . . . 269
  A. Secretory Nerves . . . 269
  B. Morphological Changes in the Pancreas . . . 272
§ 5. The Liver and the Secretion of Bile . . . 272
  A. General Phenomena of Hepatic Secretion . . . 272
  B. Dependence of the Secretion of Bile upon the Blood Supply . . . 273
  C. The Discharge of Bile in Digestion . . . 275
§ 6. The Glands of the Intestine . . . 276
  A. Glands of the Small Intestine . . . 276
  B. The Glands of the Large Intestine . . . 277
Third Section: Movements of the Alimentary Canal . . . 278
§ 1. Mastication . . . 278
§ 2. Sucking . . . 279

PAGE
§ 3. Deglutition . . . 279
§ 4. Movements of the Stomach . . . 283
A. Kneading Movements . . . 283
B. Evacuation of the Stomach . . . 285
C. Vomiting . . . 286
§ 5. Movements of the Intestine . . . 286
Fourth Section: Digestion in the Different Divisions of the Alimentary Canal . 290
§ 1. Digestion in the Mouth . . . 290
§ 2. Digestion in the Stomach . . . 291
§ 3. Digestion in the Intestine . . . 294
§ 4. Formation of Fæces and Defecation . . . 298

CHAPTER VIII.—Absorption . . . 301
§ 1. Absorption in General . . . 301
§ 2. Absorption of Carbohydrates . . . 303
§ 3. Absorption of Fat . . . 304
§ 4. Absorption of Proteid . . . 305
§ 5. Absorption of Mineral Substances . . . 307

CHAPTER IX.—Respiration . . . 310
First Section: Movements of Respiration . . . 310
§ 1. Elasticity of the Lungs and Intrathoracic Pressure . . . 310
§ 2. Inspiration . . . 312
A. Registration of Respiratory Movements . . . 312
B. Movements of the Ribs . . . 314
C. Movements of the Diaphragm . . . 316
§ 3. Expiration . . . 317
§ 4. The Number of Respiratory Movements. . . . 318
§ 5. Exchange of Air in the Lungs . . . 319
§ 6. Concomitant Respiratory Movements . . . 321
§ 7. Special Forms of Respiratory Movements . . . 321
§ 8. Pressure Changes in the Respiratory Passages . . . 321
§ 9. The Respiratory Sounds . . . 322
§ 10. Means of Protection for the Lungs . . . 323
Second Section: Innervation of Respiration. . . . 323
§ 1. The Efferent Nerves . . . 323
§ 2. The Respiratory Center . . . 325
§ 3. Respiratory Reflexes . . . 327
A. Reflexes through the Vagi . . . 327
B. Fibers from Anterior Parts of the Brain to the Medulla . . . 329
C. Other Respiratory Reflexes . . . 330
§ 4. Normal Stimulation of the Respiratory Center . . . 331
Third Section: The Blood Gases . . . 333
§ 1. Absorption of Gases in Liquids . . . 334
§ 2. The Blood Gases . . . 335
A. Nitrogen and Argon . . . 335
B. Oxygen . . . 335
C. Carbon Dioxide . . . 337
D. The Quantity of Blood Gases . . . 339
E. The Distribution of Blood Gases between Corpuscles and Plasma . 340
Fourth Section: The Respiratory Exchange of Gases. . . . 340
§ 1. Mechanism of Exchange between Blood and Alveolar Air . . . 340

PAGE
§ 2. Exchange of Gases between Blood and Lymph 342
§ 3. Changes Produced in the Respired Air 342
§ 4. The Absolute Amount of Respiratory Exchange 345

CHAPTER X.—The Lymph and Its Movements 347
§ 1. Chemical Properties of the Lymph 347
§ 2. Movements of the Lymph 348
§ 3. The Formation of Lymph 349
§ 4. The Lymph Glands 352
§ 5. Absorption from Serous Cavities 353

CHAPTER XI.—The Influence of the Organs on One Another 355
§ 1. The Osmotic Phenomena 355
§ 2. Internal Secretions 356
A. General 356
B. The Testes 357
C. The Ovaries 358
D. The Thyroid Gland 358
E. The Pancreas 362
F. The Adrenal Bodies 364
G. The Pituitary Body 367
H. The Kidneys 367
I. The Spleen 368

CHAPTER XII.—The Final Decomposition of Foodstuffs in the Body 369
§ 1. The Final Destruction of Proteid 369
§ 2. The Decomposition of Carbohydrates 374
§ 3. The Decomposition of Fat. 376

CHAPTER XIII.—The Excretions of the Body 378
First Section: The Urine and Its Excretion 379
§ 1. The Urine 379
A. The General Properties of the Urine 379
B. Composition of Urine 381
§ 2. The Excretion of Urine 384
A. Structure of the Kidneys 384
B. Mechanism of the Excretion of Urine 386
§ 3. Micturition 390
A. The Ureters 391
B. The Urinary Bladder 391
Second Section: Excretion through the Skin 394
§ 1. The Sebaceous Glands 394
§ 2. Excretion of Sweat 395
A. Composition and Properties. 395
B. The Excretory Process 396
§ 3. The So-called Insensible Perspiration 397

CHAPTER XIV.—Animal Heat and Its Regulation 398
§ 1. The Temperature of the Human Body 398
§ 2. The Source of Animal Heat 402
§ 3. Loss of Heat from the Body 403
§ 4. Protection against Loss of Heat 404
§ 5. Regulation of the Body's Temperature 406
A. Regulation of Heat Loss 407
B. Centers for Heat Regulation 408

PAGE
CHAPTER XV.—Functions of Cross-striated Muscles . . . 410
First Section: General Physiology of Muscle and Nerve . . . 410
§ 1. Fundamental Laws of Nervous Activity . . . 410
§ 2. The Properties of Resting Muscles . . . 412
A. Elasticity . . . 412
B. Chemistry of Muscle . . . 413
§ 3. Stimulation of Muscles and of Nerves . . . 414
A. The Muscle Curve . . . 414
B. Rate of Transmission of a Nerve Impulse . . . 417
C. Mechanical Stimulation of Nerves . . . 418
D. Electrical Stimulation of Muscle and Nerve . . . 418
E. Effect of a Rapid Series of Stimuli . . . 428
F. Voluntary Contractions . . . 430
§ 4. Signs of Activity in Muscle and Nerve . . . 431
A. Electrical Phenomena . . . 431
B. The Muscle Tone . . . 434
C. The Chemical Alterations in Muscle Due to Its Activity . . . 434
D. Mechanical Work . . . 435
E. Heat Formation in Muscle . . . 439
§ 5. The Central Innervation of a Skeletal Muscle . . . 440
§ 6. Fatigue and Recovery of Muscles and Nerves . . . 441
A. General Phenomena . . . 441
B. Fatigue of Human Muscles and Nerves . . . 443
§ 7. Rigor Mortis . . . 447
§ 8. Smooth Muscles . . . 447
Second Section: Reciprocal Relations between the Muscles and Other Organs of the Body . . . 448

CHAPTER XVI.—On Sensations in General . . . 451
First Section: Qualitative Relations between Stimulus and Sensation . . . 451
Second Section: The Quantitative Relations between Stimulus and Sensation . 455
§ 1. Weber's Law . . . 456

CHAPTER XVII.—The Sensory Functions of the Skin . . . 458
§ 1. Sensations of Temperature . . . 458
§ 2. Pressure and Touch . . . 461
§ 3. The Local Sign . . . 463
§ 4. Pain . . . 465

CHAPTER XVIII.—Organic Sensations . . . 469
§ 1. Motor Sensations . . . 469
§ 2. Physiological Significance of Motor Sensations . . . 472
§ 3. The Semicircular Canals and the Otolith Sacs of the Inner Ear . . . 473
A. Anatomical . . . 473
B. Experimental Suppression of the Semicircular Canals . . . 476
C. Artificial Stimulation of the Semicircular Canals . . . 479
D. The Otolith Sacs . . . 481
E. Observations on Men . . . 481

CHAPTER XIX.—Taste and Smell . . . 483
§ 1. Sensations of Taste . . . 483
§ 2. Sensations of Smell . . . 486

PAGE
Chapter XX.—Hearing, Voice, and Speech 489

First Section: Auditory Sensations 489
§ 1. Stimuli Appropriate for the Organ of Hearing 489
A. Loudness 489
B. Pitch 489
C. Timbre 491
§ 2. Transmission of Sound in the Ear 493
A. The External Ear 494
B. The Middle Ear 494
§ 3. Excitation of the Auditory Nerve 498
A. The Resonators in the Cochlea 498
B. Objections to the Resonator Theory 501

Second Section: Physiology of Voice and Speech 502
§ 1. Action of the Laryngeal Muscles 502
§ 2. Voice Production 504
§ 3. Registers of Voice 504
§ 4. Elements of Speech 506
A. Vowels 506
B. Consonants 507

Chapter XXI.—Vision 508

First Section: The Eye as an Optical Instrument 508
§ 1. The Optical Constants of the Eye 508
§ 2. Images upon the Retina 513
A. Direct and Indirect Vision 514
B. The Light-perceiving Layer of the Retina 514
C. Visual Angle and the Limits of Vision 517
§ 3. Static Refraction in the Eye 519
§ 4. Optical Defects of the Eye 520
A. Transparency of the Media of the Eye 521
B. Form of the Refracting Surfaces 522
C. Astigmatism 522
D. The Angle between the Line of Vision and the Optical Axis . . 525
E. Chromatic Aberration in the Eye 526
F. Summary 527
§ 5. The Iris. 527
§ 6. Accommodation 529
A. Range of Accommodation 529
B. Mechanism of Accommodation 530

Second Section: Excitation of the Retina and Visual Sensations 536
§ 1. Light Rays 536
§ 2. The Phenomena of Excitation 537
A. Fatigue and Recovery of the Visual Organ 539
§ 3. Sensations of Color 541
A. Relations of the Properties of Light to the Different Constituents of the Retina 541
B. Successive Color Induction 542
C. Color Mixture 542
D. On the Theory of Color 544
E. Simultaneous Contrast 547

PAGE
Third Section: Movements of the Eyes and Visual Perceptions 549
§ 1. Action of the Eye Muscles 549
A. Limits of the Eye Movements 551
§ 2. Significance of the Eye Movements for the Outward Projection of Visual Perceptions 552
§ 3. Binocular Vision 555
A. Correspondence of the Two Retinæ 555
B. Single Vision with Two Eyes 555
C. Perception of Depth 556

CHAPTER XXII.—The Physiology of the Nerve Cell and of the Spinal Cord . . . 559
§ 1. General Considerations Concerning the Finer Structure of the Nervous System 559
§ 2. The Structure of the Spinal Cord 562
§ 3. Kinds of Nerves 564
A. Classification According to Function 564
B. Special Properties of Different Kinds of Nerve Fibers 565
C. Magendie's Doctrine 565
§ 4. Functions of the Nerve Cell 566
A. The Nutritive Functions of Nerve Cells 567
B. Physiological Stimuli of Nerve Cells 569
C. Mode of Reaction of Nerve Cells to Stimulation 570
D. Dependence of the Nerve Cell upon the Blood Supply, and the Effects of Poisonous Substances 572
E. Morphological Changes in the Nerve Cell. Reproduction and Regeneration 574
§ 5. Reflex Processes 575
A. Segmentation in the Central Nervous System 575
B. General Features of Reflexes 576
C. Inhibition of Reflexes 577
D. Augmentation of Reflexes 579
E. Reflex Responses to Different Stimuli 580
§ 6. Automatic Excitation 580
§ 7. Tonus 581
§ 8. Central Functions of Peripheral Nerve Cells 582
§ 9. Centers in the Spinal Cord 585
A. Control of Skeletal Muscles 586
B. Influence of the Spinal Cord on the Vegetative Functions . . . 587
§ 10. Conducting Pathways in the Spinal Cord 588
A. Electrical Stimulation of the Cord 588
B. Methods of Determining the Conducting Pathways in the Spinal Cord. 589
C. Anatomical Data Concerning the Conducting Pathways of the Cord . 591
D. Experimental and Clinical Observations on the Conducting Pathways in the Spinal Cord 595

CHAPTER XXIII.—Physiology of the Brain-stem 599
§ 1. General Survey 599
A. Method 599
B. Divisions of the Brain 601
§ 2. The Medulla Oblongata, or After-brain 602
§ 3. The Cerebellum 605

PAGE
§ 4. The Mesencephalon, or Midbrain 613
  A. The Corpora Quadrigemina 613
  B. The Crura Cerebri 614
§ 5. The Diencephalon, or 'Tweenbrain 617
§ 6. Functions of the Brain-stem as a Whole 618

CHAPTER XXIV.—Physiology of the Cerebrum 629
First Section: The Motor and Sensory Areas of the Cortex 632
§ 1. The Motor Areas 632
  A. General Survey 632
  B. Stimulation of the Motor Cortical Areas in Different Mammals . . 633
  C. Direct and Crossed Effects of Stimulation of the Motor Cortical Areas 640
  D. The Commissures between the Cortical Areas of the Two Hemispheres 641
  E. Cortical Epilepsy 641
  F. Suppression of the Motor Cortical Areas 643
  G. The Course of the Conducting Pathways from the Motor Cortical Areas to the Nuclei of the Motor Nerves 647
  H. Development of the Motor Areas of the Cortex 648
§ 2. Influence of the Cerebral Cortex on the Vegetative Processes of the Body 649
§ 3. The Sensory Cortical Areas 650
  A. Area of General Sensation and Touch 651
  B. The Cortical Areas of Taste and Smell 653
  C. The Auditory Area 654
  D. The Visual Area 655
  E. Recapitulation 658
Second Section: Psycho-physical Functions of the Cerebrum 658
§ 1. The Significance of the Motor and Sensory Cortical Areas 659
§ 2. The Language Faculties 661
§ 3. The Association Centers of Flechsig 665
  A. Anatomical 666
  B. The Anterior Association Center 668
  C. The Posterior Association Center 669
  D. Final Survey 670
§ 4. The Time Consumed by Psycho-physical Processes 673
Appendix: Nourishment of the Brain 676

CHAPTER XXV.—Physiology of Special Nerves 680
§ 1. Cranial Nerves 680
§ 2. Spinal Nerves 682
  A. Sensory Nerves 682
  B. Motor Nerves 682
§ 3. The Sympathetic Nerves 685
  A. Relations of the Sympathetic Nerves to the Central Nervous System. 685
  B. Course of the Sympathetic Fibers 687
  C. Regeneration in the Sympathetic System 689
  D. Afferent Nerves in the Sympathetic System 689

CHAPTER XXVI.—Reproduction and Growth 691
First Section: Reproduction 691
§ 1. The Male Sexual Organs 691
  A. The Testes 692
  B. The Accessory Sexual Glands 692
  C. Erection and Ejaculation 693

PAGE
§ 2. The Female Sexual Organs 695
A. The Ovaries and Oviducts 695
B. The Uterus 696
C. Pregnancy and Birth 697
D. Innervation of the Sexual Organs 700
§ 3. Secretion of Milk 700
A. The Milk 700
B. Secretion of Milk 703
Second Section: Growth of the Human Body 705

LIST OF ILLUSTRATIONS[1]

FIG. PAGE

1.—Illustrating the use of the graphic method in recording the contraction of a frog's muscle (drawn for this edition) 6
2.—Muscle curves recorded on the same drum 7
3.—The mercury manometer 8
4.—Blood pressure curve of rabbit 8
5.—Membrane manometer (courtesy of Prof. W. T. Porter) 9
6.—Kymograph with "endless" paper 9
7.—Electric signal used as time marker 10
8.—Curves of blood pressure in left ventricle and aorta of the dog 11
9.—Recording tambour of Marey 11
10.—Receiving tambour for pulse record 12
11.—Pulse curve from carotid of man 12
12.—Capillary electrometer 13
13.—Action currents of dog's heart 13
14.—*Polystomella venusta* 17
15.—*Thalassicola nucleata* 18
16.—Parenchyma cells from root cortex of *Frittilaria* 21
17.—Leaf showing starch formation 23
18.—Root of bean with Bacteria tubercles 23
19.—*Gromia oviformis* 35
20.—*Amœba polypodia* 35
21.—Phases in the life history of *Amœba* (from Mill's "Animal Physiology") 36
22.—White blood corpuscle of frog with bacillus ingested 37
23.—*Vampyrella spirogyræ* 37
24.—*Frontana leucas* (courtesy of Prof. Gary N. Calkins) 41
25.—Chlorophyll bodies in *Lemna triscula* 42
26.—Mode of movement of *Amœba* 43
27.—Amœboid movements of white blood corpuscles 43
28.—*Vorticella* (from Mill's "Animal Physiology") 44
29.—Demarcation current in a muscle 47
30.—Electric apparatus of cramp fish (from Mill's "Animal Physiology") 49
31.—Illustrating chemotaxis 54
32.—Motor response in *Paramæcium* (courtesy of Prof. Gary N. Calkins) 55
33.—Distribution of Bacteria in sunlight 57
34.—Effects of constant current on the shrimp, *Palæmonetes* 60
35.—*Opalina ranarum* 61
36.—Cross section of intestinal musculature of cat 62
37.—A shoot of *Antennularia antennina* 64
38.—Crystals of serum albumin 69
39.—Face mask for respiration experiments 85

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[1] Unless otherwise stated the illustrations in this edition are the same as in the third German edition.

FIG. PAGE
40.—Schema of Atwater-Benedict respiration calorimeter (courtesy of Prof. Francis G. Benedict) 86
41.—Respiration apparatus of Pettenkoffer and Voit (drawn for this edition) . . 87
42.—Respiration apparatus of Sondén and Tigerstedt 88
43.—Three experiments on elimination of urea by fasting dogs 101
44.—Elimination of N in urine of man 102
45.—Preparations from the liver (normal and diabetic) of man 126
46.—Blood crystals 150
47.—Absorption spectrum of oxyhæmoglobin 151
48.—Absorption spectrum of hæmoglobin 151
49.—Hæmin crystals. 153
50.—Schema of the circulation 162
51.—Cross section through a fully contracted human heart 163
52.—"Krehl's cone" of fibers in the left ventricle 163
53.—Casts of ventricular cavities of ox heart in rigor mortis 164
54.—Position of atrio-ventricular valves when closed. 166
55.—Cardiographic sound 168
56.—Intracardial pressure curves of horse 169
57.—Pressure curves of right ventricle, left ventricle, and aorta of horse . . . 170
58.—Pressure curves from left ventricle and aorta of horse 171
59.—Schema illustrating Ludwig's theory of the apex beat 172
60.—Pressure curves in right auricle, right ventricle, and of apex beat (horse) . . 173
61.—Receiving tambour of Marey's cardiograph 174
62.—Curves of apex beat and carotid pulse of man 175
63.—Variations of electrical potential in human heart 179
64.—Action current of human heart 180
65.—Direct stimulation of isolated cat's heart 183
66.—Influence of temperature on isolated heart of the cat 184
67.—Cardiac nerves of dog 191
68.—Representation of pulse rate 192
69.—Depressor nerve of rabbit 193
70.—Behavior of blood pressure on stimulation of depressor nerve 194
71.—Pulse rate in man at different ages 197
72.—Flow of liquid through rigid tube of uniform diameter 198
73.—Flow of liquid through rigid tube of varying diameter 199
74.—Artificial schema of mechanics of circulation (courtesy of Prof. W. T. Porter) . 200
75.—Cubic enlargement of aorta of rabbit, increasing internal pressure 201
76.—Erlanger's apparatus for determination of blood pressure in man (courtesy of Prof. Joseph Erlanger) 203
77.—Blood pressure curve, feeble stimulation of vagus 205
78.—Blood pressure curve, medium stimulation of vagus 206
79.—Blood pressure curve, strong stimulation of vagus 207
80.—Current clock 209
81.—Hæmadomograph with air-transmission 209
82.—Velocity and pressure curves in carotid of horse 210
83.—Plethysmograph 211
84.—Plethysmographic curve 212
85.—Schema illustrating Weber's theory of pulse 213
86.—Spring of Marey's sphygmograph 214
87.—Marey's sphygmograph as used 215
88.—Radial pulse curve 216
89.—Contractile cells embracing wall of capillary 220

FIG. PAGE
90.—Capillary constricted by vasomotor influence . . . 220
91.—Apparatus for determining blood pressure in capillaries . . . 221
92.—Cubic enlargement of inferior vena cava of cat . . . 223
93.—Position of human body in which veins are stretched most . . . 226
94.—Position of human body in which veins are relaxed most . . . 226
95.—Variations of aortic pressure in dog . . . 229
96.—Respiratory variations of blood pressure, rabbit . . . 230
97.—Reflex rise of blood pressure in rabbit . . . 236
98.—Reflex fall of blood pressure in rabbit . . . 237
99.—Section of hepato-pancreas of an isopod crustacean (courtesy of Dr. Edgar F. Nolan, Philadelphia Academy of Natural Sciences) . . . 244
100.—Parotid gland of rabbit . . . 260
101.—Parotid gland of cat . . . 261
102.—Parts of a tongue gland of the frog . . . 262
103.—Hourly course of secretion of gastric juice in dog's stomach . . . 265
104.—Hourly course of the digestive action of gastric juice on proteid . . . 265
105.—Secretion capillaries surrounding parietal cells of gastric glands . . . 267
106.—The course of pancreatic secretion in man . . . 270
107.—The course of secretion in the pancreas of the dog . . . 270
108.—Enzymes of pancreatic juice, relative rate of activity of . . . 271
109.—Pancreas of rabbit as observed in living animal . . . 272
110.—Hourly course of discharge of bile into the intestine of the dog . . . 275
111.—Glands of large intestine of rabbit . . . 277
112.—Sagittal optical sections of floor of mouth and neck . . . 281
113.—Motor nerves of throat and palate of monkey . . . 282
114.—Nerves of stomach musculature . . . 284
115.—Schema to illustrate relation of longitudinal muscular fibers of intestine . . . 287
116.—Schema illustrating rhythmical segmentation of small intestine (courtesy of Dr. W. B. Cannon) . . . 288
117.—Schema illustrating antiperistalsis (courtesy of Dr. W. B. Cannon) . . . 289
118.—Successive stages in absorption of fat in epithelial cells of frog's intestine . . . 304
119.—Duodenum of mouse showing absorption of iron . . . 307
120.—Experiment on expansion of lungs of rabbit (drawn for this edition) . . . 311
121.—Pneumographic curve of man . . . 313
122.—Apparatus for registering volume of the respired air . . . 313
123.—Respiratory curve of rabbit . . . 314
124.—Thorax as seen from the right side . . . 315
125.—Schema of movements of the diaphragm, liver, stomach, and spleen in respiration . . . 316
126.—Diaphragmatic and thoracic types of respiration . . . 318
127.—Number of respirations per minute in persons of different ages . . . 319
128.—Spirometer . . . 320
129.—Respiratory curve of rabbit . . . 328
130.—Schema of Ludwig's pump for extraction of blood gases . . . 334
131.—Absorption of oxygen by horse's blood . . . 337
132.—Absorption of carbon dioxide in solution of hæmoglobin . . . 339
133.—Lung catheter . . . 341
134.—Amount of carbon dioxide expired, measured in two-hour periods . . . 343
135.—Elimination of carbon dioxide on ordinary diet and in fasting . . . 344
136.—Elimination of carbon dioxide by a boy . . . 345
137.—A myxœdematous woman . . . 359
138.—A cretinous child (from Holt's "Diseases of Children") . . . 360

FIG. PAGE
139.—Crystals of urea 382
140.—Crystals of uric acid 382
141.—Other forms of uric-acid crystals 383
142.—Hippuric-acid crystals 383
143.—Schema representing blood vessels of the kidney 385
144.—Schema representing tubules of the kidney 385
145.—The nerves of the bladder 392
146.—Portion of the preputial gland of the mouse 394
147.—The normal diurnal variations of temperature in man 399
148.—The elimination of carbon dioxide in man determined every two hours . . 400
149.—The temperature of the body after death 401
150.—Curves of extension and elastic shortening of muscle 412
151.—Apparatus of Blix and Lovén for recording the elasticity curve of a muscle . 412
152.—Extension and elasticity curves of the frog's gastrocnemius 413
153.—Fick's apparatus for recording variations in the length and in the tension of a muscle 414
154.—Simple contraction curve of the frog's gastrocnemius 415
155.—Curves illustrating the method of determining the rate of conductivity in the sciatic nerve of a frog (from a student's note-book) 417
156.—Schema representing the rheocord of Du Bois-Reymond 418
157.—Nonpolarizable electrodes (courtesy of Prof. W. T. Porter) 419
158.—Induction coil (courtesy of Prof. W. T. Porter) 420
159.—Details of the Wagner hammer, or interrupter of the induction coil . . . 421
160.—Arrangement of apparatus for sending induction shocks through a muscle (drawn for this edition) 422
161.—Catelectrotonus 424
162.—Anelectrotonus 425
163.—Stimulation of a nerve by ascending make and descending break induction shocks 426
164.—Distribution of an electric current in a human arm 427
165.—Entrance into and exit from a nerve of an electric current applied to the skin over the nerve 428
166.—Tetanus curve of the frog's gastrocnemius. 429
167.—Tetanus curves of the white and red muscles of the rabbit 430
168.—Schema representing a rheotome experiment 431
169.—Rheotome of Bernstein 432
170.—Schema representing the spread of an excitation causing an action current . 433
171.—Illustrating the theory of electrotonic currents 433
172.—Relation of work to size of stimulus 435
173.—Isotonic and simple projectile contractions 436
174.—Relation of the form of contraction curve to load 436
175.—Veratrin curve of frog's gastrocnemius 437
176.—Isotonic and isometric contractions 438
177.—Fatigue curves 441
178.—Fatigue curves (courtesy of Prof. F. S. Lee) 442
179.—Ergograph of Mosso 444
180.—Fatigue tracings obtained with Mosso's ergograph 444
181.—Fatigue tracings with different rates of stimulation 445
182.—Arrangement of cold, heat, and pressure spots on the skin of the wrist . . 459
183.—Topographical distribution of cold and heat senses 460
184.—The semicircular canals of the pigeon, laid bare 474
185.—Relation of the planes of the semicircular canals to each other 475

FIG. PAGE
186.—Distance of the anterior and posterior canals (prolonged) from each other . 475
187.—Pigeon with membranous labyrinths removed 476
188.—Pigeon five days after removal of the right membranous labyrinth . . . 476
189.—Pigeon twenty days after removal of the right membranous labyrinth . . 477
190.—The taste zone of the upper surface of the human tongue 483
191.—Course of the gustatory nerve fibers (from Leube's "Special Medical Diagnosis") 484
192.—Olfactometer of Zwaardemaker 487
193.—Seebeck's siren 490
194.—Schema representing the relations of overtones to their fundamental . . . 492
195.—Resonator of Helmholtz 493
196.—Transverse section through the left auditory canal and tympanic membrane . 494
197.—Horizontal section through the tympanic cavity 495
198.—Hammer and anvil 496
199.—The organ of Corti of the human ear 500
200.—Action of the posterior crico-arytenoid muscle 503
201.—Action of the lateral crico-arytenoid muscle 503
202.—Laryngoscopic picture during quiet respiration 504
203.—Appearance of the vocal cords while producing a chest tone 505
204.—Position of the vocal organs in producing the sound of broad A 505
205.—Position of the vocal organs in producing the sound of long E 506
206.—Illustrating the refractive index 509
207.—Illustrating the refracting surfaces of the eye 510
208.—Illustrating a simple refracting system 511
209.—Illustrating the nodal points in a complex system 511
210.—Position of the cardinal points in the schematic eye 513
211.—Section through the retina of a full-grown dog 515
212.—Illustrating the blind spot in the eye 516
213.—View of the rods and cones from the outer surface of the retina 517
214.—Diagram showing the visual angle 518
215.—The static refraction of a hypermetropic, an emmetropic, and a myopic eye . 519
216.—Method of demonstrating entoptic phenomena 521
217.—Entoptic particle in the vitreous body 522
218.—Illustrating spherical aberration 523
219.—Refraction of light rays in regular astigmatism (from Fuchs' "Text-book of Ophthalmology") 524
220.—Astigmatism chart 525
221.—Diagram illustrating chromatic aberration 526
222.—The iris of a cat at rest and on stimulation 528
223.—The iris of a cat with a sector isolated 528
224.—Method of demonstrating accommodation in the eye 530
225.—Reflection of images from the eye in accommodation 531
226.—The protrusion of the iris in accommodation 531
227.—Meridional section through the ciliary body 532
228.—Zonule of Zinn of an adult man 533
229.—Schema of the mechanism of accommodation according to Schön 534
230.—Schematic representation of the optic tracts (modified from Fuchs' "Text-book of Ophthalmology," drawn for this edition) 535
231.—Optogram formed in the visual purple 537
232.—Morphological changes produced in a frog's eye by light 538
233.—Disk with white and black sectors 539
234.—Illustrating the excitation of the retina successively by white and black sectors 539
235.—Excitation of the retina as a function of the time exposed 540

FIG. PAGE
236.—Illustrating successive color induction 542
237.—Excitation of the different components of the visual organ by light rays of different wave lengths 544
238.—Excitation of the different components in eyes of König and Dieterici by different wave lengths 545
239.—Illustrating simultaneous contrast 548
240.—The extra-ocular muscles and their axes of rotation (from Fox's "Diseases of the Eye") 550
241.—Rotation of the eye about the separate axes 551
242.—The field of vision projected on a distant plane perpendicular to the line of vision 552
243.—Illustrating Scheiner's experiment 553
244.—Illustrating optical delusion in judgment of distances 554
245.—Illustrating optical delusion in judgment of distances 554
246.—Illustrating optical delusion in judgment of distances 554
247.—The rivalry of the two retinæ 555
248.—Illustrating the simultaneous formation of images of an oblique line in the two eyes 556
249.—Showing the positions of these images on the retinæ 557
250.—Stereoscopic vision 557
251.—Brewster's stereoscope 558
252.—Ganglion cell of a leech showing intracellular networks 560
253.—Pericellular network of Golgi, nucleus dentatus of the dog 561
254.—Semidiagrammatic section of the spinal cord 562
255.—Schema of connections in the cord 563
256.—Reflex contractions of the frog's leg, illustrating summation in the nerve cells of the cord 571
257.—The relative resistance of several different nerve centers to asphyxiation . . 573
258.—Schema of an axon reflex through peripheral ganglion cells 584
259.—Schema of a reflex through several peripheral ganglion cells 584
260.—Illustrating a possible explanation of an axon reflex 585
261.—Cross section at different levels of the spinal cord 589
262.—Secondary descending degeneration in the cord 590
263.—Illustrating method of stimulating the cord electrically 590
264.—Sections through the cervical and lumbar parts of the cord 591
265.—Diagram of the course of the sensory conducting pathways (from Strümpell's "A Text-book of Medicine") 592
266.—Diagram of the upper and lower motor conducting pathways (from Barker's "Nervous System") 594
267.—Median section through the brain, showing divisions 600
268.—Transverse section of the medulla oblongata 602
269.—Position of the nuclei of the cranial nerves 603
270.—Brain of a dog with the cerebellum removed 606
271.—Diagram showing paths connecting the cerebellum and pons with the cerebrum (from Barker's "Nervous System") 610
272.—Frontal section through the anterior quadrigeminal body of a human fœtus . 615
273.—Schematic representation of the nucleus of the oculo motor nerves . . . 616
274.—The brain of *Squalius cephalus* a bony fish 618
275.—The brain of *Scyllium canicula*, a dog-shark 619
276.—The brain of a frog 620
277.—The brain of *Hatteria punctata*, a lizard (from Wiedersheim's "Anatomie der Wirbeltiere") 621

FIG. PAGE
278.—Brain of a pigeon (from Wiedersheim's "Anatomie der Wirbeltiere") . . 622
279.—Brain of a rabbit (from Wiedersheim's "Anatomie der Wirbeltiere") . . . 623
280.—Lateral view of a dog's brain (from Ellenberger and Baum's "Anatomie des Hundes") . . . 624
281.—The remainder of the brain of Goltz' dog after removal of the cerebral hemispheres . . . 625
282.—Dorsal surface of the dog's brain, with excitation points indicated according to Fritsch and Hitzig's early experiments . . . 632
283.—Latent period of muscular contraction induced by stimulation of the cortex and by stimulation of the underlying white matter . . . 633
284.—Structure of the cortex of the convolutions bordering on the fissure of Rolando 634
285.—Motor cerebral localization in the monkey, outer surface of left hemisphere (from Barker's "Nervous System") . . . 635
286.—Motor cerebral localization in the monkey, inner surface of left hemisphere from Barker's "Nervous System") . . . 635
287.—Motor cortical areas in the monkey (from Barker's "Nervous System") . . 637
288.—The motor cortical areas of the chimpanzee . . . 638
289.—Diagram of the external surface of the left cerebral hemisphere of man . . 639
290.—Diagram of the internal surface of the right cerebral hemisphere of man . . 639
291.—The course of an epileptic attack induced by stimulation of the motor cortical zone . . . 642
292.—The motor tract at various levels of the internal capsule (from Barker's "Nervous System") . . . 647
293.—Sensory areas on the outer surface of the right cerebral hemisphere . . . 654
294.—Sensory areas on the inner surface of the left cerebral hemisphere . . . 654
295.—Schematic representation of the optic tracts (modified from Fuchs, drawn for this edition) . . . 656
296.—Diagram of the speech tract together with various centers of the cerebral cortex concerned in speech (from Leube's "Special Medical Diagnosis") . . 662
297.—The myelogenetic areas of the human brain, outer surface . . . 666
298.—The myelogenetic areas of the human brain, inner surface . . . 667
299.—Curve representing the depth of sleep . . . 677
300.—Distribution of the superficial areas served by the different sensory roots (from Strümpell's "A Text-book of Medicine") . . . 683
301.—Schematic representation of the connections of the sympathetic fibers . . 686
302.—Normal curve of contraction of the uterus . . . 698
303.—Pressure curve of the last contraction of the uterus in parturition . . . 699
304.—Curves representing the height and weight of boys and girls of different ages . 709
305.—Variations in the height of military recruits in Sweden . . . 710

A TEXT-BOOK OF PHYSIOLOGY

INTRODUCTION

The aim of scientific physiology is, to determine the functions of the animal body and to derive them strictly from the elementary conditions of animal life (LUDWIG).

THE animal body is composed of a large number of different organs. The first task therefore is to find out what functions are performed by each individual organ, to learn how these functions may be influenced by different conditions, and to determine as exactly as possible the intensity with which each function may be performed under different circumstances.

Of all the varying conditions, whose influence on the functions of the organs we shall have to investigate, there is none so important as the *action of the organs themselves upon one another,* and the consequent manifold interdependence among them. It is only by giving attention to this interaction of the organs that we can arrive at any real determination of their functions, or make any satisfactory progress toward understanding how the existence and capabilities of the body as a whole result from the collective activity of the individual organs.

In most of the functions the activity of the elementary constituents of the body, the *cells* and *tissues,* is to be reckoned as a fundamental condition. And the farther modern physiology progresses, the more clearly does it appear that the cell, or as Brücke appropriately calls it, the *elementary organism,* represents the real unit of the body, not only in the morphological sense, but in the physiological sense as well. The remarkable properties of the living substance, as exhibited in most of the fundamental processes going on in the living body, are dependent upon much more complicated conditions than the exact scientific investigations of our time have been able to explain; but in most physiological problems where research has progressed far enough to warrant theoretical conclusions to any degree well founded, it has been shown that the fundamental conditions for the functions of the organs and tissues are precisely those conditions which determine the vital activity of the cells. It need scarcely be emphasized here that in so saying I have meant to give no *actual* theory, that is to say, no mechanical explanation, of the phenomena in question. If we trace the functions of the organs back to the vital activity of the cell, we have done nothing more than point out where the solution of the problem is ultimately to be sought, without having thereby entered more deeply into the problem.

I wish expressly to state that this conception does not at all imply that in the living body forces are to be found of an essentially different kind from those which rule in the inanimate world. The *fundamental point of view* of all modern natural science is this, that every phenomenon is the necessary consequence of certain active causes, which when they coöperate under the same circumstances always produce the same phenomenon. The energy which represents the active cause of any natural process is never destroyed and is never created anew; it may assume various forms, it may pass from one form to another, but in its quantitative relations it is never changed.

This *principle of the conservation of energy,* which was first enunciated by J. R. Mayer, J. P. Joule, L. A. Colding, and H. Helmholtz (1842–1847), *in physiology, as in other fields, is the foundation of all scientific thinking.* We maintain that in those processes which take place in the living body and which together make up our conception of life, the principle of the conservation of energy holds good: and in so doing we place physiological investigation on the firm basis of exact natural science, even though we are not yet in position to follow out this view to the phenomena of life in all their details, or to conjecture what is the *real cause* of the activity of living substance. This conception of the living world and of its ruling forces is quite different from the ancient *vitalism,* now finally abandoned. That doctrine relied upon a capricious phantom of vital force, which, entirely unfettered by natural law, at times was responsible for the most unheard of results, and at others vanished completely from the field.

All animals throughout the whole vast series, from the lowest to the highest, are the proper subject of physiological research. While it is true that the close relation of physiology with medicine has given man and the animals which stand next to him in the scale an exceptionally predominant place in research as well as in education, physiology does not seek to know the functions of the body and the fundamental conditions of existence in the human species alone. *Philosophically all animals possess an equal interest* for physiology; and in studying the fundamental conditions of life (cell activity and its dependence upon different variables) we are compelled to widen the province of our research still more and to draw upon the other large groups of living beings, the unicellular organisms and plants, for data looking to the explanation and completion of the results obtained from higher animals.

Moreover, it is incumbent upon physiology to study the *development* of vital phenomena both in the individual and in the animal kingdom as a whole. Thus it is placed side by side with *comparative anatomy* whose province it is to investigate the development of all organic *forms* from the lowest to the highest. We are not to forget, however, that physiology is *an exact natural science.* It is not sufficient to demonstrate how a definite function appears first in its simplest form and then becomes more and more manifold and complicated: physiology must give also a mechanical explanation. Investigation of the elementary mechanism of the phenomenon is therefore the chief and all-important thing in physiology, and if we were to name the ultimate goal of the science, we should say it is to furnish a mechanical explanation of the *origin* of living beings and of their *progressive development* to higher and higher forms. Within the province of physiology would thus fall the mechanical explanation of morphological results, and according to this conception physiology would constitute the very summit of all biological investigation. It is scarcely necessary to remark that in the present state of our knowledge we cannot yet forecast how this far-distant goal shall be reached.

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CHAPTER I

GENERAL PHYSIOLOGICAL METHOD

§ 1. PHYSICAL, CHEMICAL, AND HISTOLOGICAL METHODS

PHYSIOLOGY makes use of all the modern aids to research in natural science. We have not infrequently to employ the finest instruments of precision and the highest mathematical analysis. The physiology of the two highest sense organs, the eye and the ear, has progressed so far that every fact which relates not to our own perceptions and interpretations, but to the purely physical conditions of their origin, can be treated with a discrimination and exactness of experimentation which place this portion of physiology on a plane with the most exact of all natural sciences, namely, *physics*. The same holds, for the most part also, in the general physiology of cross-striated muscle and nerve. Here electrical science and several other branches of physics have found wide application.

The study of the circulation of the blood presents an extraordinarily complicated problem in hydraulics; the study of equilibrium and locomotion of the body is to be treated from a purely mechanical point of view; in the discussion of the respiratory exchange of gases in the lungs and in the tissues physiology turns to account both theoretically and experimentally the physical theory of gases; and the doctrine of heat regulation is based naturally on the physical theory of heat. In short, almost every division of physics has some direct bearing upon our study of the functions of the body.

In the same way *chemistry* is of far-reaching importance in physiological research. The chemical nature of the substances contained in or formed in the animal body is one of the first things to be considered. Besides this, chemical physiology has to investigate also the changes which the ingested substances undergo in the vital processes of the body.

Microscopical investigation furnishes us valuable data with regard to the activity of the cells, and *histological methods* have therefore very wide application in physiology.

The physiology of the sense organs and of the central nervous system stands in very close relation with *psychology* and the *theory* of *knowledge*, or to put it more strongly, a thoroughgoing study of this branch of physiology is impossible without a knowledge of these sciences.

Finally, physiology must take into account also the discoveries of *pathology* and of *pharmacodynamics*. For however the functions of the body are influenced by the different abnormal changes, or by poisons, they are not altered in nature; and the study of these changes must evidently throw light on the normal processes.

As for the rest, physiology must create its own methods according to the nature of the problems to be solved; and in the following presentation of the functions of the body we shall discuss as far as may be necessary for our present purposes the methods in use. There are however some general methods of physiological technique which it will be appropriate to discuss in this place.

§ 2. EXPERIMENTS ON LIVING ANIMALS

It is true that one can obtain important information concerning the functions of the organs and of the entire body *without any operative interference*—indeed, all of our direct observations on man have been made under such circumstances. But it is often necessary to make the organs accessible to immediate observation. We are therefore often compelled to perform on living animals many kinds of operations, some of which put the skill and inventive genius of the operator to a severe test. In these operations the animals are as a rule *anæsthetized* with ether, chloroform, chloral, morphine or some other narcotic. Only if the purpose of the experiment makes it necessary is the operation performed on un-anæsthetized animals. For many physiological purposes the animal must be observed for a long time after the end of the operation, and in such cases it is necessary to use the *antiseptic* and *aseptic methods* of surgery with every possible care. Furthermore, it is many times of advantage in the experiment to suppress the voluntary movements of the animal, and this is done by administering the American arrow poison, *curare*. Since this drug paralyzes the respiratory muscles along with others it is necessary to resort to *artificial respiration*, which is usually accomplished by rhythmically forcing into the lungs with a bellows a quantity of air suitable to the size of the animal. The air is introduced through the trachea by means of a cannula connected with the bellows. In all operations where the pleural cavities must be opened artificial respiration is indispensable (Vesalius, about 1540).

After the animal has been prepared in this way, the particular experiment follows. It would be impossible to describe here even in condensed form the different principles of experimentation which must be observed if perfectly unequivocal results are to be obtained. The following may be given as an illustration:

There are in general only two ways of discovering the influence of the central nervous system on a given organ or function: either the nerve supplying that organ may be cut and the effects on the behavior of the organ noted, or the nerve may be stimulated artificially and the resulting action of the organ be determined. In most cases the latter method gives the clearer results, for mere section of the nerve cannot give us any definite conclusions, unless the nerve at the moment it was cut was actually transmitting impulses from the central system, which of course is by no means always the case.

It is often of great profit, in determining the physiological importance of an organ, to *extirpate* it, and to maintain the animal alive. The resulting absence of certain phenomena frequently permits of very valuable conclusions. Especially is this true in the case of organs like the thyroid gland and the adrenal bodies, which to direct observation disclose no sign of their func-

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tions. Extirpation and transsection represent important methods of research in studying the functions of the central nervous system. It cannot be denied however that the results of excision methods are unfortunately too often very difficult of explanation, and that their interpretation is not infrequently made still more difficult by unintentional lesions.

§ 3. EXPERIMENTS ON SURVIVING ORGANS

In the *cold-blooded animals many organs remain alive* for a long time after the death of the organism, even when they have been cut out of the body. By virtue of this property it has been possible to collect a great mass of most important facts. Our knowledge of the general properties of nerve and muscle rests for the most part on experiments with exsected organs. Organs removed from the body remain still longer alive if, as was first done by Ludwig and his school, they be artificially nourished with blood. Under such conditions it is possible also to maintain organs of warm-blooded animals alive for a considerable time after death of the body as a whole. Organs removed from the body which remain capable of activity are called *surviving organs.*

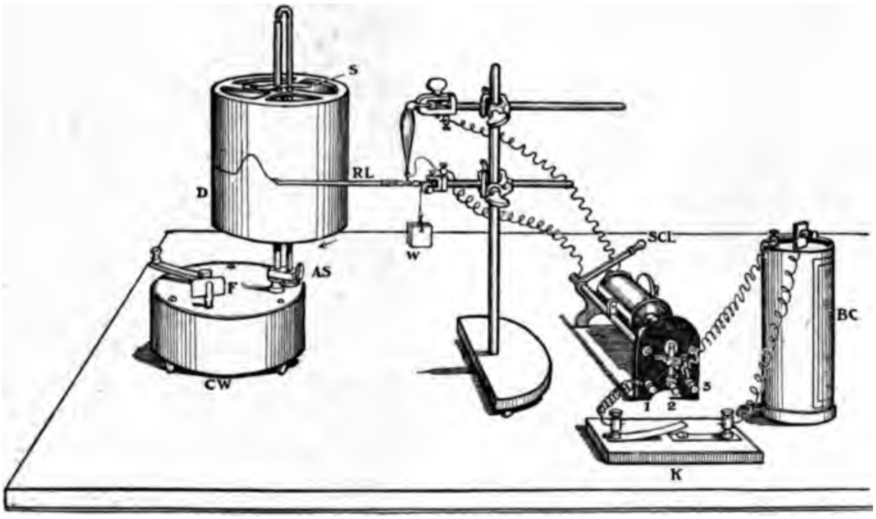

FIG. 1.—Illustrating the use of the graphic method in recording the simple contraction of a frog's muscle. For description, see text.

§ 4. THE GRAPHIC METHOD

Functions of organs are not infrequently expressed by outward movements of some kind, which as a rule are so rapid that their details cannot be followed by the naked eye. They can be studied very exactly, however, if one can hit upon a method by which the *movements record themselves* upon a moving surface (graphic method, Ludwig, 1847).

Since this method finds very wide application in most branches of physiology, it is necessary to describe it here somewhat fully. The apparatus employed for recording movements by the graphic method consists essentially of two parts: (*a*) the surface upon which the movement is traced, and (*b*) the mechanism by which the movement is transferred to the recording surface.

A. THE KYMOGRAPH

[A very simple illustration of the graphic method is given in Fig. 1, where the simple contraction of a frog's muscle is being recorded on a moving surface—an application of the method first made by Helmholtz in 1852. In such an apparatus[1] the surface consists of a glazed paper covered evenly with the soot from a gas-flame and attached to the surface of the drum (D) of an instrument called the *kymograph*. The drum is caused to revolve in the direction of the arrow by a clockwork (CW) inclosed in the base of the kymograph. The clockwork is propelled by a strong spring which is wound by means of the lever at the left. By means of the thumbscrews (AS) and fans (F) of different sizes, the gearing of the clockwork may be so adjusted as to revolve the drum at any desired speed.

The *recording lever* (RL) terminates in a fine point which bears on the smoked surface, and, as the drum revolves, scratches a tracing in the soot. The muscle, the gastrocnemius of a frog, is so prepared that its tendon of Achilles is free to be attached to the hook on the lever. The other end of the muscle is still attached to the femur, a stump of which is left to be fastened in the clamp. In order to imitate as nearly as possible the action of the muscle in its normal relations, it is necessary that it be made to lift some weight (W)—i. e., to do a certain amount of work. This weight, however, has considerable inertia compared with the lever itself, and in order that this may influence the character of the contraction as little as possible, the weight is fastened to the lever quite close to its axis, the muscle itself being fastened somewhat farther from the axis. Electrical connections are made so as to send a shock through the muscle.

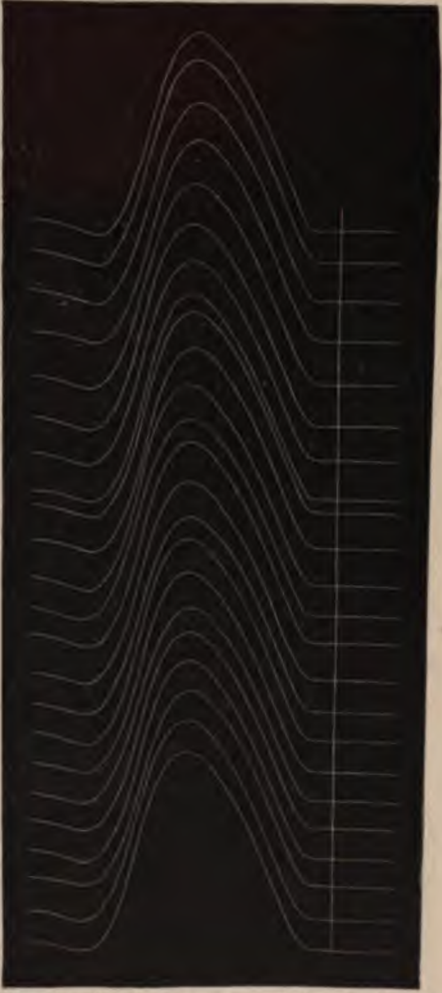

FIG. 2.—Muscle curves recorded one above the other on the same drum; to be read from right to left. The vertical line marks the moment of stimulation.

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[1] For the sake of simplicity the recording surface in the figure is shown white, and the tracing black.

When the muscle is thus caused to contract, it lifts the lever and a "muscle curve," or myogram, the proportions of which are determined by the extent of the contraction and the speed of the drum, is recorded.—ED.]

When it is desired to compare with one another several successive contractions of the same or of different muscles, the curves may be recorded one above another by simply lowering the drum on its supporting axis to different levels. Such a series is shown in Fig. 2.

Tracings made in this way are preserved for future study by immersing the smoked paper for a moment, after it has been cut loose from the drum, in a solution of shellac in wood alcohol. The alcohol evaporates quickly, leaving a permanently hard varnish over the soot.

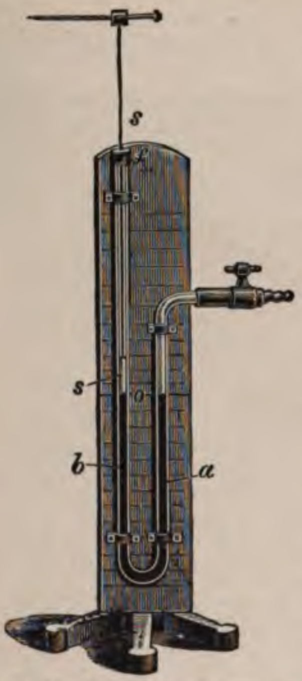

FIG. 3.—The mercury manometer, provided with a writing point for recording the level of the mercury in the limb (*b*) of the tube.

The graphic method is adapted for recording a great many other physiological phenomena. The first use made of it on an extensive scale was that of recording the blood pressure and its variations (Ludwig, 1847).

The blood pressure in an artery may be determined by tying a cannula into the central cut-end of an artery and connecting it with a U-shaped tube containing mercury (mercury manometer, Fig. 3). When the connections are properly made and the artery is unclamped, the blood pressure is brought to bear on the mercury column in the limb (*a*) of the tube, and the column in the other limb (*b*) is forced upward. This difference, however, is never

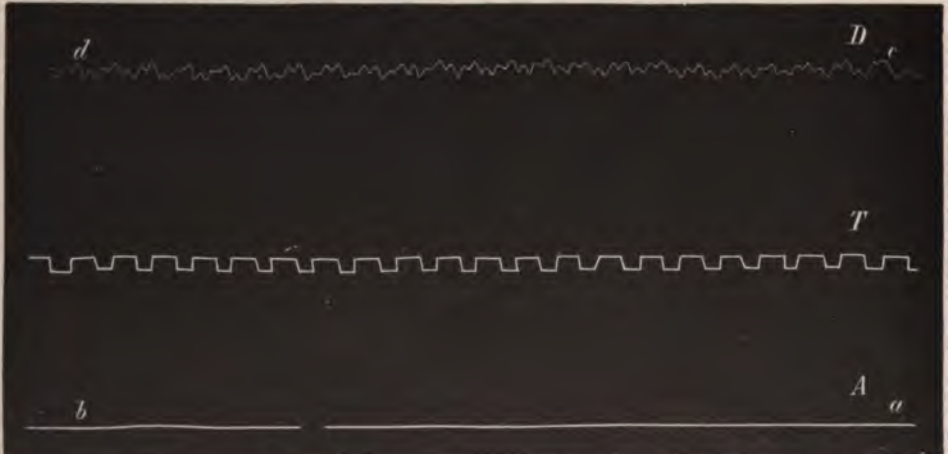

FIG. 4.—Blood pressure curve taken from a rabbit. *A*, the line of no pressure; *T*, the time recorded in seconds; *D*, the pressure tracing. To be read from right to left.

constant but shows incessant variations corresponding to the heart beats, respiratory movements, etc. These variations produce oscillations in the mercury column, which are recorded by placing on the free surface of the mercury a float (*s*) to which is attached a light rod carrying at its upper end a writing point. The writing point is adjusted so as to scratch a tracing on a lightly smoked, revolving drum. Fig. 4 represents a tracing (*D*) of the blood pressure in a rabbit recorded in this way. (For further explanation of this experiment, see Chapter V.)

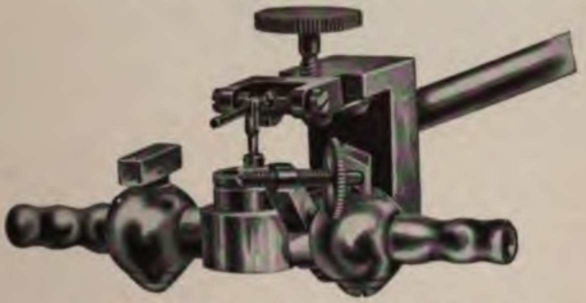

FIG. 5.—A membrane manometer, after Porter.

Owing to the inertia of the mercury column, the actual variations of pressure are not exactly reproduced by this method. They may be more faithfully portrayed if the blood pressure can be brought to bear on an elastic membrane or spring (elastic manometer). [Fig. 5 shows such a manometer. A small chamber about 7 mm. in diameter is provided with two stopcocks, one of which is connected with the artery the pressure in which is to be measured, while the other opens to the atmospheric air. This chamber is closed above by an elastic

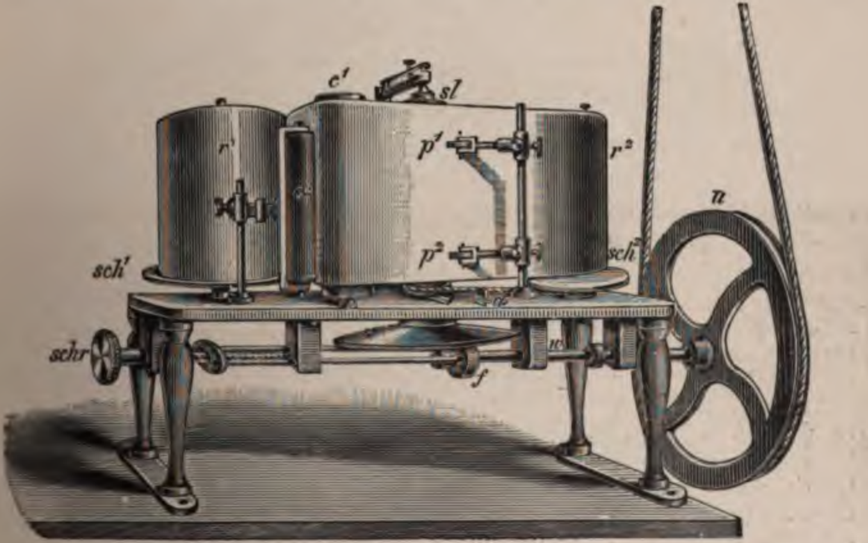

FIG. 6.—A kymograph with "endless" paper, after Ludwig and Baltzar.

membrane (not shown) upon which is fastened by means of cement a small disk supporting a rod which carries a magnifying lever. The height of the writing point, which is fastened to the lever, may be varied by means of the thumbscrew at the top. Errors due to inertia of the blood-column itself may be still further diminished by damping its movements with the stopcock between the chamber and the artery. A thumbscrew at the right enables one to graduate this resistance as required.—Ed.]

In case it is desired to continue the record of the blood pressure or of other physiological movements uninterruptedly for a long time, a kymograph carrying two drums, placed at some distance from each other and so arranged that the smoked paper extends around both, may be employed, and a longer recording surface is thus obtained. A still longer record can be made in ink on a white surface by means of a kymograph carrying "endless" paper (Fig. 6). By means of a "pen" of suitable construction, a record can be continued for days, the paper being unrolled from one spool and rolled onto another at the proper rate of speed, after the ink has had time to dry.

B. TIME RECORDERS

It is often necessary to know the speed at which the revolving surface passes the writing point. This may be determined roughly by regulating the revolutions of the drum to a certain uniform speed; but if the exact temporal relations of the events which are being recorded must be known, it is necessary to employ a *time marker*. This instrument commonly takes the form of an electric signal.

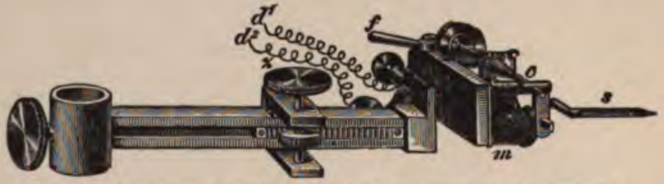

Fig. 7.—An electric signal used as a time marker, after Deprèz.

A convenient form is that represented in Fig. 7. An electro-magnet (m) bears on its armature a recording lever (s) which can be arranged so as to write on a smoked surface. The movements of the armature, and hence those of the lever, are determined by making and breaking the current to the magnet at regular intervals of time. If it is desired to mark seconds, as in Fig. 4, a clock beating seconds may be so arranged as to make and break the current. If small fractions of a second are required as in Fig. 8, a *tuning fork* vibrating the desired number of times per second may be made to dip a platinum wire in and out of mercury with each vibration and so interrupt the current.

The tuning fork itself may also be employed as the time marker by attaching a very light writing point to one of its prongs and arranging this so that it will make a light tracing on the recording surface while the tuning fork is in vibration.

It will be apparent: (1) that the time interval to be employed must be adapted to the speed of the drum and this in turn to the rapidity of the events to be recorded; and (2) that while it is not necessary to have the drum move at a uniform speed, if the time record is made simultaneously with the physiological record, much more satisfactory results will be obtained if it does move both uniformly and steadily.

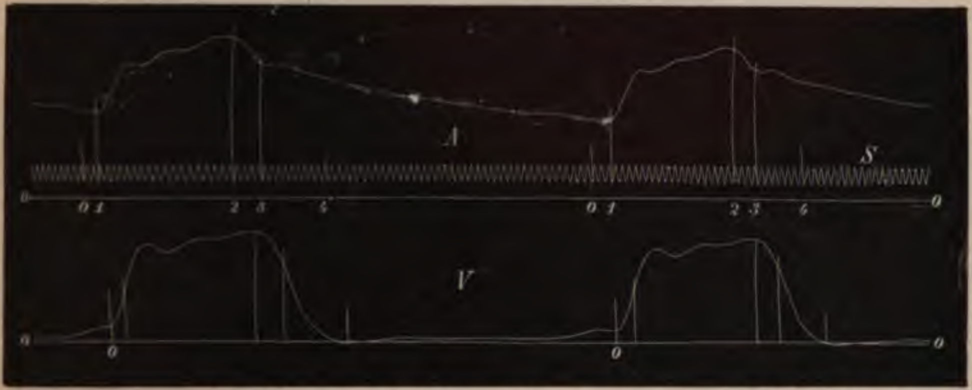

FIG. 8.—Curves of blood pressure in the left ventricle (*V*) and in the aorta (*A*) of the dog, after Hürthle. *S*, the time-record in $\frac{1}{100}$ths of a second. To be read from left to right.

C. RECORDING BY AIR-TRANSMISSION

The method of air-transmission for the registration of physiological events, first introduced into physiology by Buisson (1861) and later brought to perfection by Marey, has also found wide application. The principles of this method may be understood from the following:

When two thin-walled rubber bulbs are connected with each other by means of a rubber tube having fairly rigid walls, and pressure is exerted on the one, the other will of course be dilated. Now if a writing lever be connected with one of the bulbs it can be made to record any such variations in pressure taking place in the other. The apparatus necessary for registration by air-transmission

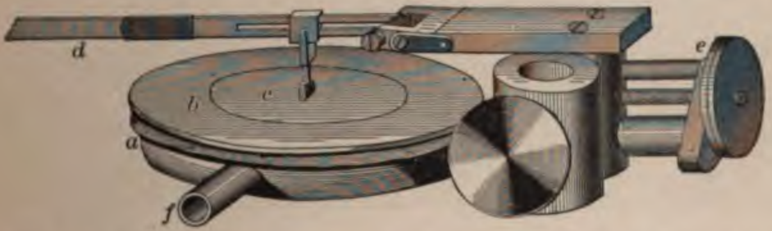

FIG. 9.—Recording tambour of Marey, actual size. *a*, metallic case; *b*, thin India-rubber membrane; *c*, thin disk of aluminium supporting the lever *d* (a small portion of which only is represented); *e*, screw for placing support of lever vertically over *c*; *f*, metallic tube communicating with cavity of tambour for attachment to an India-rubber tube.

consists therefore of two parts: a *receiving* bulb or tambour, and a *recording* bulb or tambour.

A very simple form of *recording tambour* is shown in Fig. 9. A hollow aluminium tube (*f*) conveys the air-waves to the elastic membrane (*b*) fitting over the chamber. A small metallic disk (*c*) is cemented to the membrane and on the upright bar as a fulcrum rests the writing lever (*d*). The axle of the lever is held in a yoke, the distance of which from the fulcrum can be readily adjusted and the excursions of the writing point be thereby varied as desired.

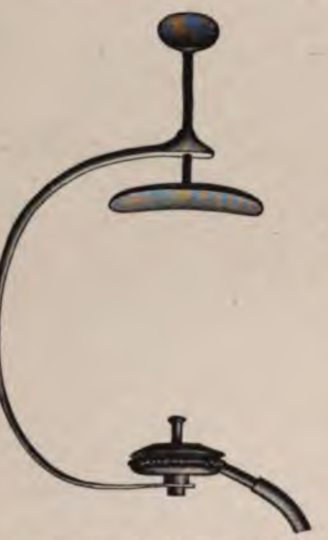

FIG. 10.—Receiving tambour adapted for taking a pulse-record from the carotid artery of man.

The second part of the apparatus or *receiving tambour* is usually in the form of a small rubber balloon or of a small metallic box covered with a rubber membrane. The form of the recording tambour can be the same for a great many kinds of physiological movements, but the form of the receiving tambour must be adapted to the special form of experiment in which it is being used.

The receiver shown in Fig. 10 is adapted for transmitting movements of the wall of the carotid artery, for the purpose of securing a pulse-tracing. It consists of a small metallic box containing three small spiral springs, which serve to give the membrane covering it a certain tension. The membrane bears on its outer side a small button or plunger which can be applied to the skin over the artery. The pulsatory movements of the arterial wall are taken up by the plunger and are conveyed by the tube leading from the chamber of the box to the recording tambour. The whole apparatus is fastened to the neck by means of the hoop and screw.

With well-constructed apparatus this method of registration has been found to be very exact. But not all tambours are so constructed, and it is necessary before undertaking any exact determinations to prove the apparatus. A very good test for a recording tambour is that of registering a pulse curve, the pulse-beat being received from the carotid artery by an apparatus of given form. With the receiver shown in Fig. 10 the tracing given by the carotid should be essentially like that shown in Fig. 11.

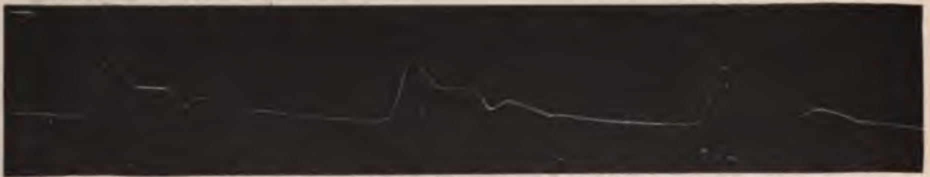

FIG. 11.—Pulse curve from the carotid artery of man, after Edgren. To be read from left to right.

D. REGISTRATION BY PHOTOGRAPHY

Even the most delicately constructed writing lever has some weight, and hence, because of its inertia, may give an incorrect form to the curve. The ideal recorder would be entirely without mass. We have such a recorder in a beam of light, provided the experiment can be so arranged that the movement to be recorded is transmitted directly to a small mirror which reflects the beam of light, and the reflected beam can then be made to fall on a moving surface which is sensitive to light.

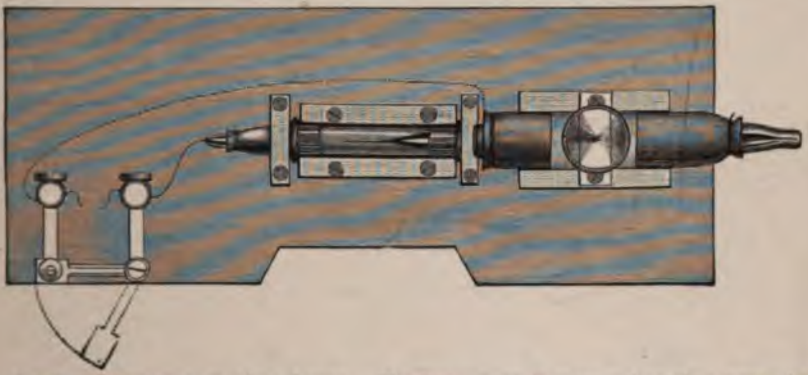

FIG. 12.—Capillary electrometer, after Lovén. The instrument is mounted so that it can be placed on the stage of a compound microscope.

But the *photographic method* is of much greater importance for recording movements which cannot be recorded in any other way.

This is the case, for example, with the excursions of the *capillary electrometer*. This instrument (Fig. 12) consists of a fine capillary tube partially filled with mercury and dipping into a dilute solution of sulphuric acid so that the mercury comes in contact with the acid in the tube. When electricity from any source is led into the instrument by connecting one pole with the Hg and the other with the H_2SO_4, the mercury meniscus in the capillary tube will move in the direction of the current. Such movements can be magnified by a microscope and be recorded on a moving photographic plate. Since many forms of activity in the animal body are accompanied by electrical changes of potential which cannot be demonstrated in any other way than by a very sensitive electrometer, this mode of registration is very valuable for the study of such phenomena. Fig. 13 represents the photographic curve of the electrical variations (action currents) appearing during the cycle of events in the dog's heart.

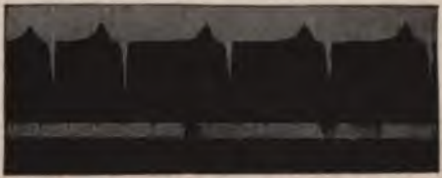

FIG. 13.—Action currents of the dog's heart as recorded by photographing the excursions of the mercury column in the capillary electrometer, after v. Kries. Electrical connection was made with the base and apex of the heart. First phase: base negative to the apex. Second phase: apex negative to the base. The upper line represents the time in fifths of a second. To be read from left to right.

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CHAPTER II

THE CELL

§ 1. GENERAL CONSIDERATIONS

A. THE CELL AS AN ELEMENTARY ORGANISM

THE remarkable substance whose activity is the basis of all vital phenomena in both animals and plants, and which we call therefore the *living substance*, occurs not in a homogeneous aggregation but in the form either of discrete masses called cells or of small bodies which represent transformed cells (Schleiden, 1838; Schwann, 1839). Every living being and every separate cell arises from a preëxisting cell (*omnis cellula e cellula*, Virchow, 1855). Many animals and plants throughout their lives consist of but one cell. In others, from the original cell new ones arise; these in their turn multiply, are transformed into a variety of shapes, and thus become adapted for special purposes. In this way the independence which characterizes the single-celled creatures is reduced to a considerable extent, so that cells detached from the parent organism are as a rule unable to maintain themselves.

The cell is therefore the *beginning* and the *source* of the entire body, and the formed elements of which the body is constructed are each and all nothing else than cells or cell derivatives. Correspondingly we may say that the powers of the body as a whole represent the sum of the powers resident in the individual cells and the cell descendants.

In the study of vital processes we have thus in the first place to consider the activity of cells. The discoveries, however, which have been made by direct observation upon cells (especially those that are free-living) are not by any means sufficient to serve as the basis for a complete presentation of the general vital phenomena. Besides, there take place in the many-celled organisms, owing to the differentiations occurring in them, many kinds of phenomena which do not take place in the elementary organism, or which at least with our present means cannot be demonstrated, and at all events can be investigated much more thoroughly in the organs of the many-celled animals. In any general discussion of vital phenomena, therefore, one should give the results obtained in the different provinces of general physiology each its proper share of attention. Since, however, this text-book has for its special subject the physiology of man, I must limit myself in the present chapter to the *boldest outlines* of general physiology. Elsewhere the general vital phenomena will be discussed from time to time in connection with the facts of special physiology.

We know nothing at all about how life first appeared on the earth, and we are unable to attach any great importance to the hypotheses which have been put forward concerning its origin. For a long time it was imagined that many kinds of living creatures arose directly from dead matter by *spontaneous generation.* But the more deeply studies in this direction were followed, the more improbable this view became, and at last it was held only with reference to the lowest organisms; until finally Pasteur (1861) by his ingenious researches incontestably established the fact that spontaneous generation does not take place at all.

Within the cell the living substance is divided between the *nucleus* and the surrounding *protoplasm.* The protoplasm may be manifoldly differentiated into contractile fibers, cilia, etc. Besides, the cell contains in greater or less quantity nonliving substances of the most different kinds, some of which appear clearly as specialized contents—e. g., the cell-sap of plant cells and the fat of fat cells—while some are intimately mixed with the nucleus or protoplasm and are therefore not to be distinguished from living substance.

Some cells are surrounded by a specialized *cell membrane,* while others have none; hence it is not an essential constituent of a cell. Almost all plant cells have even in their early stages a specialized membrane which increases in thickness as the cell grows in size. According to present views it represents either a transformation product of the outer layer of the protoplasm or a secretion product of the cell. Only a few *animal cells* have an actual membrane. The zona pellucida of the egg cell, the membrane of fat cells and probably the sarcolemma of muscle fibers are about all that can be named. In other animal cells however the outermost layer of the cytoplasm is often firmer and more elastic than the inner parts, and is therefore able to protect the cell to a certain extent in the same manner as a true membrane.

Cells differ greatly in external *form.* The spherical form which we regard as the type is by no means general: we find on the contrary a great variety of forms, not only in the many-celled organisms, where the shape of the cell is influenced by its position with reference to other cells, but also in free living, isolated cells. Cells likewise vary in *size,* all the way from that which is perceptible only with the highest magnification of the microscope to that of the giant cells of certain algæ, many meters in length.

The *nucleus* occurs usually as a spherical or oval body in the middle of the cell; but it may take many other forms. As a rule the size of the nucleus bears a direct proportion to the size of the cell. The larger the cell is, the larger is the nucleus. However, there are many exceptions to this rule also. Most cells contain but a single nucleus, although not infrequently two or more may be present. Indeed, in the giant cells of the bone-marrow, in several of the lowest organisms, and in some other cells, as many as one hundred nuclei have been observed.

B. THE RECIPROCAL RELATIONS BETWEEN THE NUCLEUS AND PROTOPLASM

Most animal and plant cells are nucleated. Only in the Bacteria is the presence of a nucleus doubtful. Some authors claim indeed that these organisms also are to be added to the general cell scheme; but the facts which have been brought forward in support of this view are far from sufficient to constitute actual proof. Although the *red blood corpuscles* of the Mammalia contain a nucleus at an early stage of their development, in their mature state they are, so far as we know, without nuclei. If so, they are scarcely to be regarded as cells, since having lost the nucleus they are no longer capable of reproduction.

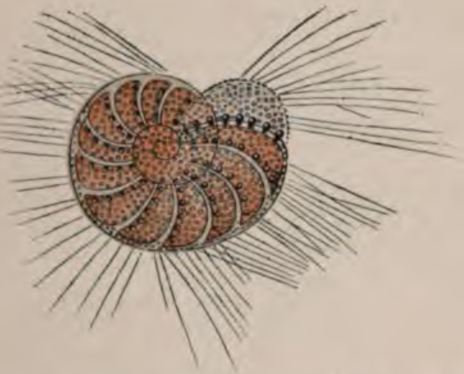

FIG. 14.—*Polystomella venusta*, a microscopic organism surrounded by a calcareous shell, after Max Schultze.

Wherever it occurs the nucleus represents a necessary constituent of the cell. Single-celled forms may be divided by a sharp cut or by other means into a nucleated and a nonnucleated part. The former is soon regenerated to a complete cell even if it contain but a portion of the nucleus; while the nonnucleated part invariably dies after a short time, for although it may move about quite normally, may ingest foreign bodies (Infusoria), and even kill them, no digestion, or at best only a partial digestion, can take place (Nussbaum).

The *production of certain substances* on the part of the protoplasm is likewise stopped by the removal of the nucleus. A nonnucleated portion of *Polystomella* (Fig. 14) is no longer able to elaborate calcium carbonate, while a nucleated piece at once makes good any defect in its calcareous shell by the deposit of new carbonate at the injured place (Verworn). In plants it has been observed that an isolated piece of protoplasm is unable to construct a new cellulose membrane (Klebs).

By the influence of a *low temperature* on the cell of *Spirogyra* caught in the act of division, Gerassimow succeeded in driving all the nuclear substance into one daughter cell, leaving the other quite devoid of a nucleus. In a series of such experiments it was seen that in twenty-one days the growth of the enucleated cells amounted to 0.4–4.5 per cent of the average growth of the normal cell, while the growth of the cells with a surplus of nuclear material exceeded that of the normal cells by as much as seventy-eight per cent. At the same time the solution of starch in the enucleated cells either did not take place at all or proceeded very feebly; the outer cell membrane was less extensible than usual; the color of the chlorophyll bands became constantly paler and their contour less clear.

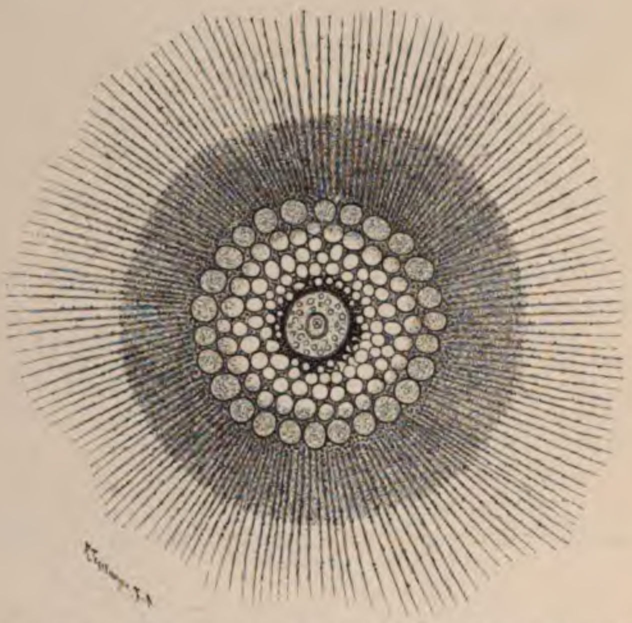

FIG. 15.—A radiolarian, *Thalassicola nucleata*, after Verworn. Cross section of a normal individual. The layers from without inward are: the corona of radial pseudopodia, the gelatinous layer, vascular layer, pigmented sheath about the central capsule, and the central capsule (in the center).

While the nucleus is thus of the greatest importance for the normal activity of the protoplasm, it cannot maintain an *independent existence*. When the protoplasm is paralyzed with narcotics the nucleus may indeed continue its movements (Demoor), showing itself quite as independent of the protoplasm as the protoplasm is of the nucleus. Nevertheless, if removed entirely from the protoplasm, even if it be entirely uninjured by the manipulation and be protected from all external disturbances, as has been done in the case of the great radiolarian, *Thalassicola* (Fig. 15, Verworn), the nucleus invariably perishes without exhibiting any trace of regeneration. Nor do nuclei ever occur in nature without a protoplasmic sheath; it may be extremely thin in certain cells, but it is never entirely wanting.

Many hypotheses have been advanced to explain the influence of the nucleus and the nature of its reciprocal relations with the protoplasm, but they are yet rather more of a speculative than of an exact scientific nature. The only conclusion which can be drawn with certainty from the discoveries thus far made is *that the metabolic processes of the cell go on normally only under the mutual influence of both nucleus and protoplasm,* which after all is only a bare statement of the facts in the case.[1]

C. PHYSICAL AND CHEMICAL PROPERTIES OF PROTOPLASM

Protoplasm appears as a viscous, usually colorless substance which is not miscible with water, and which always contains a varying number of very small, punctiform granules. The distribution of the granules in the cell body is seldom uniform, for one finds as a rule an outermost layer of greater or less thickness free from them. Since this layer is firmer than the inclosed protoplasm containing granules, it is designated as the *hyaloplasm* (Leydig) in contradistinction to the granular *spongioplasm.*

In general it is assumed that resting protoplasm has an *alkaline reaction.* This appears to be true however only with indicators which are not sensitive to CO_2: for with indicators which respond to CO_2, neither animal nor plant cells in the resting state show the alkaline reaction (Friedenthal). But in the case of some lowly organisms—e. g., the fission-fungi and the Amœbæ—the true reaction of the living substance must still appear doubtful, since these are able to live in strongly alkaline nutrient media—a circumstance which does not, however, constitute conclusive proof of an alkaline reaction for the interior of the cell.

In the gelatinous, colloidal substances (e. g., a solution of gelatin which is drying up through loss of water) with which from a purely physical point of view protoplasm exhibits a close agreement, all possible gradations are met with from the fluid to the solid state, and for such substances the terms "fluid" and "solid" may have within wide limits a purely relative significance. Hence it is not difficult to understand that views regarding the *state of aggregation* of protoplasm are very divergent, it being regarded by some authors as solid, by others as fluid. Moreover, it is not to be overlooked that in the endless varieties of differentiations met with in different orders of living beings the state of aggregation may present not insignificant differences. For the cells which exhibit protoplasmic currents (cf. page 21) as well as for the amœboid cells (cf. page 42) and the egg and early embryonic cells, Rhumbler, with strict regard to the laws which apply to fluids, has adduced weighty reasons for the view that the protoplasm possesses in fact a *fluid state of aggregation,* and has the mechanical peculiarities of a foam the individual alveoli of which are locally of different constitution.

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[1] Spitzer, Loeb and R. S. Lillie have brought forward considerable evidence that the nucleus is the chief agency in the activation of oxygen within the cell.—Ed.

Water is an integral constituent of living substance and on drying the cell either dies or it becomes apparently dead ("dry rigor"), and resumes its vital activities again on the addition of water.

We do not know anything definite about the manner in which water is combined with the real living substance. That it is not held in pores of the protoplasm as in a sponge appears from the fact that water cannot be pressed out by mechanical means. No more can the water here be regarded as an analogue of the water of crystallization in inorganic salts. It seems more likely that it is held in interstices between the molecules or combinations of molecules which make up the living substance. It is not impossible also that at the death of the protoplasm a part of the water constitutes a product of disintegration.

The *specific gravity* of protoplasm is somewhat greater than that of water. It refracts light more strongly than water, is transparent in thin layers, opaque in thick layers. Some forms of living matter are *doubly refractive.* This property was first observed in cross-striped muscle (Boeck); but since that time it has been found that practically all contractile substance differentiated into fibers, such as smooth muscle cells, cilia, etc., is positively doubly refractive in such a way that the optical axis coincides with the direction of the fibers (Engelmann). This fact is evidence that the structures in question have a different molecular arrangement from that of other living structures.

We know nothing concerning the *chemical constitution of living substance.* Chemical investigation of dead animal and plant bodies has made us acquainted with a very large number of different organic and inorganic compounds: but not even the delicate micro-chemical reactions have been able to furnish any information on the chemical nature of living substance. We can only say, therefore, that when the living substance dies we are able to demonstrate proteid bodies of different kinds as the chief constituents, and that *in animals at least the living substance can be formed, as it appears, only from proteid bodies* (cf. Chapter III).

D. MORPHOLOGY OF THE CELL CONTENTS

Everywhere, in plants as well as in animals, *protoplasm has the same appearance,* just as it is everywhere essentially the same with respect to its fundamental vital properties. Even with the highest possible magnification we are unable to distinguish the protoplasm of a plant cell from that of an animal cell. *This similarity is of course only apparent,* for, since the life process in every particular organism takes place in a way peculiar to itself, and since the protoplasm—outside the nucleus—represents the theater of different vital activities, these outstanding differences must be conditioned by a difference in the quality of the protoplasm (O. Hertwig).

Leaving out of account the apparent similarity of the protoplasm, different cells may as a whole present a very different appearance. This is due partly to the external form of the cell and its envelope, which must be regarded as something secondary at least, partly to differentiations inside the cell (cilia, contractile fibers), and partly to different substances deposited within the cell. Sometimes the last are present in such quantity that on first sight the cell appears to consist only of substances foreign to protoplasm, as it is here defined.

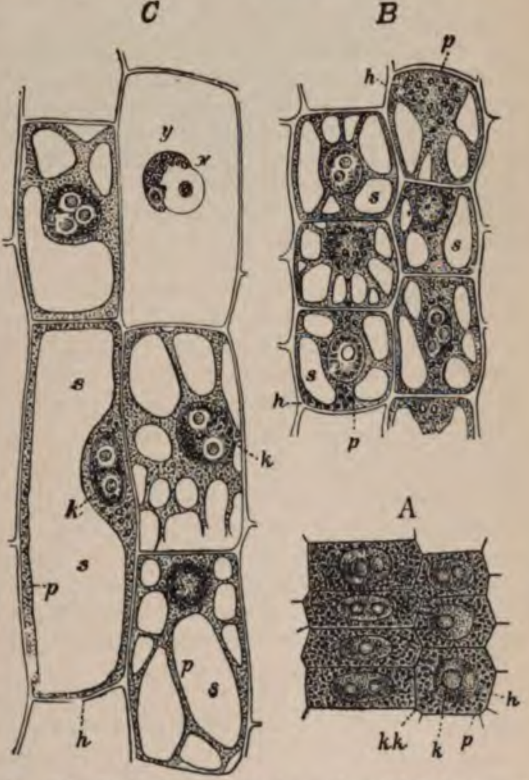

FIG. 16.—Parenchyma cells from the middle layer of the root-cortex of *Frittilaria imperialis;* longitudinal section, after Sachs. *A*, portion of the section close to the root-apex, very young cells, without cell-sap; *B*, cells of the same layer about 2 mm. from the root-apex; cell-sap (*s*) is forming in the protoplasm (*p*); *C*, cells of the same layer 7–8 mm. from the apex. The cell at the right above has been ruptured by the razor; its nucleus (*xy*) is seen much swollen by absorption of water; *k*, nucleus; *kk*, nucleolus; *h*, cell-membrane.

These *cell contents* vary a great deal in kind: substances which are taken up from outside by the cell to be further elaborated in it, substances stored in the cell as reserve material, substances formed in the cell by its own activity to be given out again under appropriate circumstances, etc.

In most plant cells the protoplasm fills but a small part of the cell body (Fig. 16). Only those cells which lie close to the growing tip consist entirely of protoplasm. In their growth the wall of the cell increases in size much more rapidly than the protoplasm, and as a result vacuoles are formed filled with cell-sap. The nucleus then lies embedded in a mass of protoplasm, which is connected by means of protoplasmic strands with a layer inside the cell walls. The protoplasm of such cells streams back and forth within the cell wall, carrying with it the granules embedded therein and ofttimes the nucleus as well.

In the protoplasm of green plant cells are contained specially differentiated *chlorophyll bodies* (cf. Figs. 25 and 31) to which these cells owe their green color, and which are of very great importance in the vital activities of plants (cf. page 23). Among the inclosures contained by the plant cell outside the cell-sap, the starch granules are to be especially mentioned, since they represent the first visible product of the assimilative activity of the plant cell.

Animal cells as a rule consist *almost entirely of protoplasm* and contain foreign substances only in relatively small quantities; they are therefore essentially like young plant cells (Fig. 16). There are some animal cells also in which the protoplasm is almost entirely displaced by foreign substances. This is the case for example with fat cells in which the major part of the fat in the body is deposited. Eggs likewise contain an abundant supply of proteid, lecithin and fat which are to serve as nourishment for the developing embryo.

Other inclosures which occur in greater or less abundance in animal cells, are: fat droplets in the cells of the mammary glands and of the intestinal mucosa during absorption; pigment granules in the pigment cells of the skin and of the choroid coat in the eye; glycogen granules in the liver cells, etc. In the naked cells which are able to take up solid particles from the surrounding medium we observe often small Algæ, Bacteria, Infusoria and the like (Figs. 19, 20, 21 and 22), which serve as nourishment for the cell, and, after digestion is completed, indigestible shells, skeletons, envelopes, etc. Again small cavities filled with fluid (vacuoles) are present in the protoplasm of certain animal cells. Among these are to be mentioned especially the so-called *contractile vacuoles*, i. e., drops of fluid which are pressed out of the protoplasm by the contraction of a surrounding sheath, only to be re-collected from the protoplasm in the same place again when the contraction ceases (Figs. 21, 24, 28).

Finally, there are found within the protoplasm of animal cells certain plant cells, Algæ, which do not serve their host as nutritive material, but merely live in company with it (*symbiosis*). They are of the greatest importance to the life of the animal cell in which they occur, since through the activity of their chlorophyll bodies, they supply it with the necessary oxygen, thereby rendering it independent of the oxygen contained in the surrounding medium. We have the most beautiful instance of symbiosis in a lichen, which is nothing more than an aggregate individual consisting of a fungus and an alga.

Reference must be made to works on cytology and histology for a discussion of the ultimate structure of the protoplasm, nucleus and centrosome, as well as for the changes in these accompanying cell division.

§ 2. THE VITAL PHENOMENA OF CELLS

A. INTRODUCTORY SURVEY

The vital activity of all cells, both plant and animal, consists of two opposite processes, assimilation and dissimilation. We include under *assimilation* all the synthetic processes, of whatever kind, going on in the cell or under its influence; under *dissimilation* all the disintegration processes going on in the cell or under its influence.

A. *Assimilation* is of two kinds, namely growth of protoplasm, i. e., formation of living substance, and syntheses of new substances not living.

Our knowledge of the growth of protoplasm is still very meager. We can observe how the cell increases in size, and how it multiplies after it has reached a certain size, but the inner mechanism of these processes is still quite obscure. Somewhat more satisfactory is our knowledge of the syntheses of organic nonliving substances accomplished by cells. In fact the synthesis which is quite the most important of all, namely, *the formation of starch* in the green parts of plants, is known with tolerable exactness, and may be described briefly as follows:

There always occur in the neighborhood of the nucleus of plant cells small, colorless, highly refractive bodies, for the most part oval or elliptical in form, which are called *trophoblasts* and which arise always, like the nucleus and the centrosome, by division of preëxisting trophoblasts. These structures generate within themselves the chlorophyll.

The property of plants discovered by Ingenhousz (1779), Senebier (1782–1800), and Th. de Saussure (1804), *of reducing carbon dioxide,* depends upon this chlorophyll. The reduction takes place under the influence of the sun's rays, and starch appears as the first visible product of the resulting synthesis. It is deposited in the chlorophyll bodies in the form of small, highly refractive granules (Julius Sachs, 1862). At the same time the plant gives off the oxygen set free by the reduction of carbon dioxide, and if it grows in a closed room the quantity of CO_2 in the confined air constantly decreases, while the quantity of O_2 is correspondingly increased.

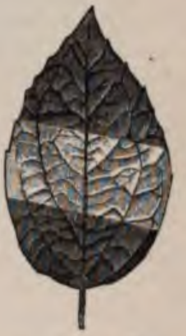

FIG. 17.—This leaf, which, in the living condition, had been partially covered with a strip of tin foil, was subsequently treated with iodine for the starch reaction. The area which had been shaded remains colorless, showing that starch cannot be formed without the direct action of sunlight, after Noll.

Starch serves as the starting point for all further synthetic processes in the plant body. By its cleavage and hydration different kinds of sugars are produced, and, this being the form in which carbohydrates are transported, they are of great importance in the further synthetic processes within the plant body. Vegetable oils are also formed from starch; and it participates finally in the synthesis of proteids in plants.

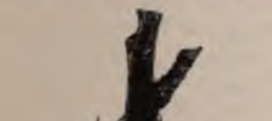

FIG. 18.—The root of the field bean (*Vicia Faba*) thickly beset with bacteria tubercles, after Noll.

Besides the elements found in starch (carbon, hydrogen and oxygen), *proteids* contain nitrogen and sulphur (some also phosphorus). The plant obtains these elements from the soil principally in the form of nitrates, sulphates, phosphates and ammonia compounds. It obtains on the other hand only an insignificant part of its nitrogen from the ammonia and nitric acid in the air. The nitrogen, sulphur and phosphorus are liberated from their compounds by processes of reduction and they together with the elements contained in starch are synthetized into proteids. It is very probable that the amino acids and their amides—e. g., asparagin (amino-succinamic acid, $C_4H_8N_2O_3$)—represent intermediate stages in this synthesis; but *how* such processes take place we do not yet know. Finally from the proteids thus formed, living protoplasm is constructed.

Certain plants are able to absorb free atmospheric nitrogen and to combine it into organic compounds. A species of bacterium, *Clostridium Pasteurianum,* which lives in the soil, is an example (Winogradsky). Krüger and Schneidewind isolated a N-combining *Bacillus* which in sixty-two days transferred 4.6–8.5 mg. of atmospheric nitrogen to proteid nitrogen. According to Kuhn one hektar of his experiment field in one year would experience through the agency of microbes alone an increase in nitrogen of 66 kg. Other microörganisms capable of fixing nitrogen are the Azobacteria studied by Beyerinck. Still others which form on roots of certain species of Leguminosæ peculiar excrescences, called root tubercles, have the power of transforming free nitrogen into such compounds (amides?) as are able to serve not only themselves but also their hosts as the immediate source of nitrogenous food (Hellriegel) (Fig. 18).

Several other *mineral constituents* are needed in the development of plants, notably: iron, which is necessary for the formation of chlorophyll; potassium and magnesium, which it is believed play an important rôle in assimilation and the syntheses of the body; calcium, which is very important in the transportation and combination of the harmful products of metabolism (oxalic acid), etc. On the other hand, the plant does not require any organic foodstuffs. If the root of a maize plant which has been germinated in water be placed in a vessel with an artificial nutrient solution (one per cent potassium nitrate, 0.5 per cent each of sodium chloride, calcium sulphate, magnesium sulphate, and calcium phosphate, and 0.005 per cent ferrous sulphate) while the foliar part is exposed to the air, the plant grows quite perfectly, develops into a large maize stalk, puts forth leaves and brings forth seed.

Only the *plants containing chromophyll*[1] have the power of feeding exclusively on purely inorganic substances. The parts of the plant devoid of chlorophyll receive their carbohydrates from the parts which contain chlorophyll. Those plants which, like the Fungi, contain no chlorophyll at all must obtain substances already completely organized for their food; and this is likewise the case with the whole animal kingdom.

The beginning of the organic syntheses going on in nature is therefore the formation of starch in the green parts of plants under the influence of sunlight. The energy stored up by this means is used in all the further processes of the plant body. In plants and plant parts lacking chlorophyll as well as in animals all the life processes take place at the expense directly or indirectly of the substances formed in the green parts of plants. *The green plants therefore constitute a necessary condition for the life of all other living beings on the earth.* But since carbon dioxide, the nitrates and sulphates required by plants are present on the earth and in the atmosphere entirely independent of the life processes of animals, plants can get along without the aid of animals.

We are not to suppose, however, that synthetic processes do not take place in animals. It is true that animals cannot form complex compounds out of completely oxidized carbon (CO_2) and hydrogen (H_2O) and that the animal body can utilize as raw material only compounds of relatively complex constitution, chief among them being proteids, fats and carbohydrates. But from this raw material *the animal body has the power of forming many new substances, notably living protoplasm, by a true synthesis.*

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[1] This term, employed by Engelmann, and adopted by the author, includes all the coloring matters in plants capable of exercising an assimilative function. Since, however, by far the most abundant coloring matter is *chlorophyll*, it will avoid confusion perhaps to use only the one term hereafter.—ED.

Besides the substances just mentioned the animal cell, like the plant cell, requires certain *mineral compounds* in order that it may develop fully and accomplish its functions in a normal manner. Thus observation on the Metazoa has proved that the animal body is continually giving off such substances in its excretions, and would necessarily become impoverished in this respect if the supply were not sufficient. Even in grown animals very profound disturbances ensue as a consequence of such failure of mineral substances, which ultimately end in death. The growing body has a relatively much greater need of inorganic compounds, for such substances are absolutely necessary for the construction of its organs.

Among the mineral substances contained in the fluids of the animal body common salt ($NaCl$) comes first in order of quantity. A solution of common salt alone, of a strength corresponding to its concentration in these fluids (0.6–0.9 per cent), is in fact sufficient to maintain a frog's muscle or a frog's heart in functional condition for a long time after its removal from the body, whereas an exsected heart will not beat in a solution where $NaCl$ is wanting (Lingle).

In a solution containing only $NaCl$, however, the contractions of the heart gradually cease, although they may be roused again by the addition of $CaCl_2$ in small quantity. The addition of KCl is likewise beneficial; but whereas the Ca salt is favorable to the *contraction* of the heart, the K salt appears to be important for its *relaxation*. The heart beats best, therefore, in a nutrient fluid in which are contained Ca and K as well as Na (Ringer, Howell and several other authors).[1]

Analogous phenomena appear in other organs. A skeletal muscle of the frog remains alive outside the body longer if $CaCl_2$ is added to the $NaCl$ solution. It is asserted, at least for smooth muscles, that the Ca salt favors the contraction process, and KCl the relaxation, just as in the heart. The egg of *Fundulus* develops in $NaCl$ solution only when $CaCl_2$ is added (Loeb).

In the present state of our knowledge of this subject it would be premature to conclude that the metals just discussed have the same sweeping importance for all animal cells. As a matter of fact data are at hand which show that such a generalization is not warranted. Thus the vibration of flagella—e. g., in the spermatozoa—and cilia of both vertebrates and invertebrates, is entirely independent of $NaCl$ in the surrounding fluid. The same is true of the contractile stalk of *Vorticella* (Fig. 28) and related Protozoa (Overton). In very young larvæ of *Arenicola cristata* solutions containing $CaCl_2$ favor muscular movements, while solutions containing $MgCl_2$ favor ciliary movements. Pure $NaCl$ solutions are much more harmful for the latter than for muscular movements; Na-free solutions stop muscular movements, whereas cilia remain active in these, and are quite unaffected by pure $CaCl_2$ or $MgCl_2$ (Lingle). In this connection should be mentioned also the facts brought out by Goldberger that certain Ca salts which have so favorable an influence in the higher animals, are poisonous for the Protista, while other Ca salts are harmless for them.

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[1] A solution especially well adapted for feeding an excised mammalian heart is the following: eight per cent $NaCl$, 0.075 per cent KCl, 0.1 per cent $CaCl_2$, 0.1 per cent $NHCO_3$, and saturated with oxygen. (Compare the composition of the blood ash, Chapter V.)

Besides the elements just mentioned (Na, Ca, K and Cl) and those contained in the proteids, fats and carbohydrates (C, H, O, N, S, P), there are still a few others which are just as necessary for the animal body. First among these are: Mg, contained with the Ca in the solid framework of the bones; Fe, which is necessary for the formation of the coloring matter in the red corpuscles; and I, which is a necessary constituent of the secretion of the thyroid gland.

In all *processes of assimilation* in nature, whatever their kind, *energy is stored up*. As a measure of the energy contained in a substance we use the amount of heat developed by its combustion. Carbon dioxide and water are not combustible substances, but starch produced from them generates a considerable quantity of heat when it is burned—possesses therefore a certain quantity of potential energy, amounting in fact to about 4.1 Cal.[1] per gram. This potential energy is derived from the sunlight, whose kinetic energy has been transformed under the influence of chlorophyll to the potential energy of starch.

When a synthesis takes place in a living cell, if the necessary energy is not supplied from without as in starch formation, the synthesis can only be carried out at the expense of potential energy stored in the cell itself. In other words: in all synthetic processes taking place in plant or animal cells without the agency of sunlight, the potential energy at the disposal of the cell is transformed in one way or another into the potential energy of the newly formed substance.

The *assimilative functions* of cells are closely bound up with dissimilative functions—i. e., if the cell has not the power to develop kinetic energy within itself no new formation of substance appears to take place—and conversely, the more rapid the dissimilative process, the more active is the assimilative process. Neither plants nor the eggs of animals can develop continuously without oxygen, as was determined successively by Spallanzani, Dutrochet, De Saussure and Schwann. In the egg of *Ctenolabrus*, a marine bony fish, the cleavage cells undergo partial solution and fuse together when oxygen is withdrawn, but are reformed when oxygen is again supplied (Loeb). Possibly in this connection belong also the facts: that growth is always accompanied by dissimilation, and that skeletal muscles increase in size only under the influence of work (involving dissimilation, cf. page 63).

B. The *dissimilative processes* constitute the source of the kinetic energy developed in the cells. These processes in plant as well as in animal cells are everywhere essentially similar, and consist in a *destruction of complex molecules*. Whether this destruction involves the living substance of the cell, or only the nonliving cell contents cannot yet be definitely decided. Under the general subject of metabolism we shall find opportunity to discuss this question somewhat more exhaustively. Here we must limit ourselves to the following:

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[1] 1 Cal. (Calorie) = the amount of heat necessary to raise 1 kg. of water from 0° to 1° C.

1. The above-mentioned destruction in a majority of cases is an *oxidation*, that is, a combustion of the substances called organic foodstuffs—proteid, fat and carbohydrate—at the disposal of the cell (Lavoisier, 1777). This is proved by the fact that all animals produce carbon dioxide, and that they succumb in a short time in the absence of oxygen. Since a plant under the influence of sunlight has the power to reduce carbon dioxide and set oxygen free, it follows that under suitable circumstances plants and animals can live if they be kept together in a closed room; for the carbon dioxide formed by the animals is reduced by the plants with the liberation of oxygen; and thus each receives the gas most useful in its life processes.

And yet we are not to suppose that the plant does not form any carbon dioxide. On the contrary the plant protoplasm in its production of kinetic energy behaves exactly like the animal protoplasm and produces carbon dioxide in the same way. The production of carbon dioxide in green plants in the light is masked by the much more abundant reduction of carbon dioxide going on at the same time; in the dark, however, where the reduction processes are checked, it is plainly perceptible.

In the decomposition brought about by the vital activity the combustible substances are not broken down immediately into their end products; but the complex organic molecules are split up gradually into less and less complex ones, oxidation and reduction processes probably taking place in rapid succession (Drechsel). Finally, these intermediate decomposition products are transformed into substances which leave the body as the end products of metabolism.

2. The *living cell itself regulates the amount of oxygen consumed*, combustion in the body being, within wide limits, entirely independent of the partial pressure of the uncombined oxygen (Pflüger).

In addition protoplasm has the power *to store up oxygen* in compounds in which it is loosely held, and from which it may be withdrawn again in case of need. This is witnessed by the fact that cells can develop kinetic energy, though in general only for a relatively short time, without a supply of free oxygen from outside. In certain cases this happens even at the expense of compounds which contain oxygen firmly bound up chemically and which cannot be deoxidized with our strongest reducing agents. We have examples of such phenomena in the Myxomycetes which continue their movements for three hours in an oxygen-free medium; in ciliated cells which can live still longer without oxygen; in the skeletal muscles which contract and give off carbon dioxide even in a vacuum. The mawworm, *Ascaris*, can live five days without a supply of oxygen (Bunge). In this case there occurs in the body of the animal a process of fermentation by which CO_2 and a mixture of valerianic acid, caproic acid, etc., are formed from the glycogen stored in the animal's tissues (Weinland). Here should be mentioned also the liberation of oxygen by hen's eggs during the first five hours of their incubation (Hasselbalch).

A very pretty experiment on the *life of higher animals in the absence of oxygen* is the following which we owe to Pflüger. At 2.44 o'clock two frogs were placed in an atmosphere cooled to about 0° C. from which every trace of oxygen had been carefully removed. At three o'clock they showed the most pronounced dyspnœa but no convulsions. They soon became motionless, as if they wished by suppression of their movements to obviate the need for oxygen.

From time to time they wandered about the cage, raised their heads and occasionally gasped. At eight o'clock they had become still more quiet and were visibly very much exhausted, but on pricking them with a wire they still showed indubitable signs of physiological integrity. On the following morning at nine the frogs lay quite motionless. Even the most vigorous stimulus failed to produce any trace of reaction and there were no signs of respiratory movements. At ten after a duration of seventeen hours the confinement was terminated and oxygen was admitted. When after two hours' exposure to the atmospheric air, and after repeated inflation of the lungs there was no sign of returning life, Pflüger opened the body cavity of one frog and found the *heart still beating with great energy* and the arteries full of remarkably bright red blood. In spite of this there were no muscular movements for five or six hours. Reflex irritability gradually returned, and spontaneous respiratory movements; but coördinated movements such as are mediated only by the higher nerve centers did not reappear at all.

3. Finally, *certain organisms* of the lowest order, especially some of the Bacteria, *can maintain life permanently only in the absence of oxygen* (anærobic Bacteria, Pasteur). The yeast cell furnishes us some information concerning the way in which the energy necessary for the functions of these organisms is liberated. This organism can maintain life for a long time without air and can develop considerable activity which displays itself notably in the alcoholic fermentation of sugar—i. e., by splitting grape sugar into $2(CO_2)$ and $2(C_2H_6O)$. Since now the calorific energy of the alcohol formed is less than that of the sugar destroyed, a certain quantity of energy is developed and is placed at the disposal of the yeast plant (Hermann, Kühne).

In the dissimilatory processes of the cell the nutrient substances at its disposal are gradually consumed, and if no supply from outside is kept up the cell must of course die of hunger.

The changes appearing in the cell body when it is deprived of nourishment have been closely followed by Wallengren on the ciliate infusor *Paramœcium*. During the first days of starvation all the food vacuoles and food masses disappear. Thereupon the small granules present in the protoplasm are consumed, and the endoplasm consequently decreases in quantity. At the end of this period the living substance of the endoplasm is itself probably consumed in part. In spite of the more or less profound changes in the form of the body thereby produced, the ectoplasm, the contractile vacuoles and the cilia are still not influenced in any noticeable way. During this period the activity of the last-named structures is maintained by material supplied by the endoplasm. With further inanition the endoplasm becomes much vacuolated, the ectoplasm, as well as a large number of the cilia become more and more absorbed, and the macronucleus is finally attacked, while the micronucleus remains comparatively untouched. At last the point is reached where everything which the cell body can furnish as nutrient material is consumed, the living substance remaining is itself exhausted, and the cell, fallen into granular disintegration, perishes.

C. *Temperature.*—Since temperature exercises a very *profound influence on the various activities* of cells, it will be appropriate to consider it in this preliminary survey. We may safely assert that for every cell there is a definite temperature which is most favorable to its life processes. The cell perishes if the temperature passes beyond certain limits, although these limits differ with different cells and may be gradually changed more or less for each particular cell by training.

For most animal and plant cells the *upper limit of temperature* compatible with life is from 40° to 47° C. They die if they be subjected even for a short time to a temperature a little higher than this, owing partly at least to the coagulation which takes place at this temperature. And yet there are cells which are able to endure a considerably higher temperature. In the hot springs of Ischia, Algæ live at a temperature of 53° C., and it is said that between the filaments of *Oscillaria,* ciliate Infusoria and Rotatoria survive a temperature of 81° to 85° C. (Ehrenberg). Many Bacteria thrive at a temperature of 50°–55° C. or even as high as 72° C.; and still more resistant against heat are their spores, a dry heat of 140° C. maintained for at least three hours being necessary to destroy life in them with absolute certainty.

With regard to the *lower limit of temperature* compatible with life, it has been found that Amœbæ placed upon ice will cease all movements and remain quiescent until the temperature is raised. If however they be frozen up in drops of water, warming fails to revive them.

A temperature below 0° C. is *not necessarily fatal* for the cell. Pictet observed with certainty that fish which had been cooled in a block of ice to − 15° C. survived after carefully raising the temperature, although their companions while frozen could be reduced to powder like ice. Fish which were cooled to − 20° C. could not be revived. Frogs survived a temperature of − 28° C., and myriopods − 50° C. Seeds of cereals do not lose their power of germination if they be subjected for a long time to a temperature of − 42° C. (C. de Candolle). Cholera spirilla and anthrax spores can be kept alive for from twenty hours to seven days at the temperature of liquid air (− 183° to − 192° C.). Indeed one species of *Bacterium* (*B. phosphorescens*) survived a period of ten hours at − 252° C. (McFadayen).

One would suppose *a priori* that at a temperature so low that the protoplasm becomes rigid, life must be temporarily suspended. According to the experiment with the fish stated above this does not appear to be correct, for in this case it would be a matter of indifference, so far as external signs go, whether the temperature of a frozen fish were − 15° or − 20° C., and yet after cooling to − 20° it dies. If life were actually suspended at − 15° it would be difficult to understand why a further lowering of the temperature has any effect. In any case we may say that at these low temperatures life processes are reduced to the minimum.

If the chemical constitution or the temperature of the surrounding medium be altered and the cells continue to live, various changes in their properties may be induced, which, especially in the pathogenic microörganisms, are of great importance, because the *degree of their virulence* may be thereby increased or diminished (Pasteur). The protective inoculation introduced by Pasteur is based upon these facts.

After this general discussion we shall now proceed to the different *manifestations of life,* taking up in order the ingestion of food, digestion, the oxidative processes, the elimination of decomposition products, the secretions, and finally the phenomena of motility, production of light, formation of heat and the generation of electricity.

B. THE INGESTION OF FOOD

It is self-evident that the medium in which elementary organisms live must contain all the nutrient substances, including oxygen and water, necessary for their subsistence. Besides, different cells have very different requirements with respect to the chemical constitution of the medium, and these peculiarities are conditioned, in part at least, upon the hereditary traits of the species.

Certain unicellular organisms are adapted for life in fresh water, others for life in salt water. Most of them die if they be placed in distilled water. Likewise if the chemical composition of the medium in which the cells live be changed suddenly, they die; but if the change take place gradually and slowly, they can adapt themselves to the altered nature of the medium and continue to live. How great a change may be made before disturbances in the vital activities of the cell appear, depends partly upon the nature of the cell and partly upon the substance added to the medium.

That even in the higher animals and man the properties of the cells are altered by a changed composition of the lymph follows directly from observations on diseases characterized by chronic intoxication (e. g., alcoholism, morphinism).

In multicellular animals the cells are bathed by a fluid, the lymph, which represents *the medium in which they live.* If the lymph is to be adapted to its purpose, it must contain in the first place all the substances necessary for the nourishment of the cells, and must possess also the other necessary chemical and physical properties.

Lymph is distinguished from those media in which unicellular organisms live, by being inclosed within the body and by being formed essentially through the activity of the cells themselves. The quantity of lymph is not unlimited, for the supply of nutrient materials and oxygen which it contains at any given time is soon used up, and their place is taken by decomposition products which are harmful to the body. But in order to maintain life in the Metazoa it is necessary in the first place that the lymph shall be always of normal constitution. To this end many organs of the body coöperate, each being adapted for a special purpose.

Experience teaches us that in general a special function cannot be carried out by a single organ, but requires the coöperation of several. All those organs which together accomplish a definite purpose are designated as an organ system or apparatus.

In order that the lymph may serve as the medium for the vital activities of the cells, it must contain besides water certain combustible substances and certain mineral constituents (all of which are comprehended under the name foodstuffs) and oxygen. Neither the foodstuffs nor the oxygen come directly into the lymph; to bring them there not less than three organ systems must coöperate: namely, (1) the circulatory system, (2) the digestive system, and (3) the respiratory system.

The object of the *circulatory system* is to supply the lymph with nutrient substances and with oxygen. The object of the *digestive system* is to take up the foodstuffs necessary to the maintenance of the body and to change them so that they may be transferred to the blood. The *respiratory system* supplies the blood with the oxygen necessary for combustion in the body.

The decomposition products arising from combustion must not remain in the lymph, because, if they did, they would finally poison the cells. They must therefore be removed by passage first into the blood and thence out of the body through the *excretory organs*.

In order that these necessary functions shall be directed to the proper end of maintaining life, they are all subordinated to the influence of the *nervous system* whose important object it is to control the organs and to regulate their functions. In addition to this, in the warm-blooded animals a *constant body temperature*—i. e., a constant temperature of the lymph is maintained through the influence of the nervous system.

1. Cells completely surrounded by membranes can take up only *gaseous and dissolved* substances. The processes concerned in the absorption of gases by the elementary organisms are but little known, and the phenomena accompanying these processes in the higher animals are fully discussed in Chapter IX. Our knowledge has progressed somewhat further concerning the absorption of fluids and compounds in solution, and since the phenomena of osmosis figure prominently in this connection, it seems best to discuss them here somewhat in detail.

Osmosis.—When a layer of pure water is carefully stratified upon a solution—e. g., sugar in water—the layers do not remain separate. The sugar begins at once to rise in spite of the force of gravity and to diffuse into the water; and the movement ceases only when the sugar is distributed uniformly throughout the whole volume of water. The same thing occurs if the water and the sugar solution are separated by a partition which is equally permeable for both. The dissolved substance passes from the place of higher concentration to the place of lower concentration just as if no separating membrane were present.

Quite a different order of things prevails if between the water and the solution a partition is interposed which allows the water but not the dissolved substance to pass through. Such "semipermeable" walls are obtained by soaking a porous clay cell in a solution of copper sulphate, carefully pouring this out and filling the cell with a solution of potassium ferrocyanide. There is then formed within and upon the clay wall a coherent layer of copper ferrocyanide through which water can be filtered; but if one attempt to filter through it a sugar solution, a much higher pressure is required, and what finally comes through is not the sugar solution at all but pure water.

If a cell prepared in this way be filled with a sugar solution and be closed by means of a stopper through which connection is made with a manometer, and the cell then be placed in pure water, an increase in pressure inside the cell is noticed, which finally rises to a definite maximum value. This value represents *the osmotic pressure of the fluid inside the cell*, and is equal to the gas pressure which would be exerted by the same quantity of sugar in the form of a vapor inclosed within the same space at the same temperature. For a one-per-cent solution of cane sugar at 13.7° C. the osmotic pressure amounts to 0.691 atmospheres. A four-per-cent sugar solution raises the pressure to 2.74 atmospheres.

Since there is no membrane which is semipermeable for all substances, it is necessary to resort to indirect methods of determining the osmotic pressure of some solutions. One such method which has found wide application both in physiology and medicine is based upon the fact that in a watery solution the dissolved substance, e. g., salt, exercises a restraining influence on the freezing of the water and consequently lowers the freezing point. The cause of this restraining influence is that the particles of salt by means of the attraction they exercise on the particles of water tend to prevent the latter from cohering with one another, i. e., from passing into the solid state. The greater this attraction, the more difficult is it for the water to be solidified, and the lower must be the temperature before this change of state can be brought about.

The lowering of the freezing point, which is designated with "Δ," is therefore a measure of the osmotic pressure (P) of the salt, calculated in atmospheres according to the formula $P = 12.03\ \Delta$. A one-per-cent solution of NaCl freezes at −0.606° C.: the lowering of the freezing point is therefore 0.606. If one finds for an unknown fluid $\Delta = 0.606$, its osmotic pressure corresponds to that of the one-per-cent NaCl solution, and amounts to $12.03 \times 0.606 = 7.29$ atmospheres.

When equimolecular quantities of different substances (i. e., quantities proportional to their molecular weights) are brought into solution in the same solvent, and solutions which have the same number of molecules of the dissolved substances in equal volumes are thus obtained, these solutions have at any given temperature the same osmotic pressure.

We have in the electrolytes an apparent exception to this law. The osmotic pressure is higher than it ought to be according to this general statement. This is due to the fact that the substances in question are partially dissociated in water into electrically charged atoms or ions—e. g., HCl into + H and − Cl, KCl into + K and − Cl, NaOH into + Na and − OH, etc. In this way the number of effective molecules in a solution is increased and in consequence the osmotic pressure is raised—in perfect agreement with the general law.

The degree of dissociation depends primarily upon the concentration and upon the nature of the dissolved substance. The more dilute the solution the more complete is the dissociation with one and the same electrolyte—i. e., the greater is the relative (not the absolute) number of free ions. In different electrolytes dissociation presents certain variations into which we cannot enter at this time. It will suffice here to say that the most important salts in the body, those formed by the alkalies with monobasic acids, are dissociated in dilute solutions of equivalent concentration to a very considerable extent, and are dissociated equally.

The combined osmotic pressure of several substances in the same solution is equal to the sum of the pressures of the separate substances.

When two solutions of different osmotic pressure are separated from each other by a semipermeable membrane, water passes from the one of less pressure to the one of higher pressure until the two are of equal pressure—i. e., are *isotonic*. With reference to each other these solutions are said to be *hypotonic* and *hypertonic* respectively.

Dead animal and plant membranes are as a rule permeable to water and, though in less degree, to substances soluble therein. When such a membrane separates water from an aqueous salt solution, the former passes into the solution and the salt passes out until the osmotic pressure on both sides of the membrane is the same. This is the case also when two isotonic solutions of different salts—e. g., NaCl and NaNO, are separated by the membrane. The common salt passes from one to the other and vice versa, so that the two solutions remain isotonic. If they are of unequal osmotic pressure—i. e., *anisotonic*—to begin with, an exchange of water and salt molecules takes place until a condition of equilibrium is established.

From these discoveries on the phenomena of osmosis it follows that every change in the constitution of the medium surrounding the cell or of the fluid contained within it will have power to effect a change in the osmotic pressure prevailing in the cell. This would mean also a change in the quantity of fluid (degree of turgescence) as well as in the chemical constitution of the fluid contained in the cell, or indeed in the constitution of the protoplasm itself, according as the limiting layer of the protoplasm is permeable or not to the substances present.

Plant cells afford us the simplest examples of the influence of osmosis. The cell membrane is permeable to gas, water and solutions. In the living cell the membrane is impregnated with water; hence all substances which are dissolved in the water can penetrate the membrane and thus come into contact with the outer layer of the protoplasm (primordial sheath) just inside the membrane (cf. Fig. 16).

Within the plant cell and surrounded by the primordial sheath we find the cell sap, which is a watery solution of various salts, carbohydrates, etc. The primordial sheath is permeable to water, but prevents entirely the entrance of certain compounds, behaves toward them in other words exactly like a semipermeable membrane.

If therefore the cell is bathed by a solution of a compound whose osmotic pressure is greater than that of the cell sap, water passes out of the cell, the primordial sheath is loosened and shrinks away from the cell membrane (*plasmolysis*). But if the cell is bathed by pure water, the water can pass through the primordial sheath in the reverse direction and raise the internal pressure above its usual level, whence we have the condition of *cell turgor.*

The primordial sheath permits the entrance of certain other substances more or less easily, and in the commerce between the cells, where transportation and exchange occur freely, it has the *power to change its permeability* according to circumstances. From this it follows that neither absorption nor excretion on the part of plant cells is to be described as a simple osmotic process.

In the *cells of the animal body,* both the cell body and the nucleus permit certain substances dissolved in water to pass through, but exclude others; they behave toward these substances like semipermeable membranes (Hamburger, Hedin). To one and the same substance the permeability of different kinds of cells may be considerably different, and it appears to vary with the same kind of cells under different physiological conditions (Hamburger).

From the investigations of Hamburger, Hedin, Koeppe and Gryns on the *permeability of red blood corpuscles* to different substances, one may gather that the K, Na, Ca, Sr, Ba, Mg ions, the different kinds of sugar, arabite and mannite do not penetrate them at all; and that they are but slightly permeable to amino acids (glycocoll, asparagin, etc.). In fact they appear to offer a powerful resistance to the amido group in the amino acids, but toward the amido group in the acid amides (acetamide, etc.) the resistance is not so great. The red blood corpuscles are permeable to NH_4 ions, to free acids and alkalies, and to alcohols in inverse proportion to the number of hydroxyl ions in the molecule; also to aldehydes, ketones, ethers, esters, antipyrin, amide, urea, urethan, bile acids and bile salts. The leucocytes of the blood and of the lymph glands, so far as this property has yet been studied, are shown to be permeable to chlorine, sulphuric acid, carbon dioxide, iodine, bromine, oxalic acid, phosphoric acid, salicylic acid, benzoic acid, and arsenic acid (Hamburger and v. der Schroeff).

Overton has studied the permeability of *cross-striated muscle* to a large number of organic compounds, and has come to the conclusion that toward the same substances they behave just as do plant cells. All compounds which are plainly soluble in water and are also soluble in ethyl-ether, in the higher alcohols, in olive oil and similar organic solvents, or which at least are not much more difficultly soluble in these than in water, penetrate living muscle fibers and other animal and plant cells very easily. But the more the solubility of a compound in water exceeds its solubility in one of the organic solvents, the more slowly does it penetrate these structures. For explanation of this peculiar behavior, Overton has put forward the hypothesis that the limiting layers of the protoplasm are impregnated with a fatty substance, a mixture of lecithin and cholesterin, and that the elective solvent power of this mixture for definite substances governs the pure osmotic permeability of the cells.

Out of some 75,000 organic compounds known at present more than 60,000, to accept Overton's rough estimate, can penetrate the cell. Among these however are found neither the carbohydrates nor a number of other substances participating actively in the metabolism of plants and animals. Overton remarks that so far as the constitution of these compounds is known, derivatives of them can always be found which do penetrate the cells very easily. How far his explanation applies to the living body we do not know.

It has been found that *different Infusoria* are to a great extent independent of the osmotic pressure of the solution, since they can exist for days at a time in distilled water, without suffering noticeably and without exhibiting any very striking changes in form (Goldberger). The eggs of *Fundulus* also do not swell if they are suddenly brought from sea water into distilled water; and they do not shrink if the reverse change is made (Loeb). McCallum found in the case of the medusa, *Aurelia*, that the salt content of the surrounding medium can vary within wide limits without materially affecting the body fluid. The fluid pressed out of the body contains less SO_3, MgO, and Na_2O, and more Cl, Fe, and especially K than the sea water; the depression of the freezing point also was less for the latter than for the body fluid. While the salt content of the blood of the green crab increases and decreases with that of the sea water, the relation in the crayfish is just the reverse: here the depression of the freezing point of the blood is 0.8° C., while in the surrounding water it is only 0.02°–0.03° C. (Fredericq). Frogs kept for weeks in distilled water give up only a part of their salt to the water, notwithstanding that between them and the water there is a difference of osmotic pressure amounting to about two atmospheres (Durig).

In the *different tissues* of any given animal also there are noteworthy differences with respect to osmosis. Membranes consisting of only a single layer of connective tissue coated with a single layer of smooth muscle cells, like the peritoneum and the mesentery, offer very little resistance to the passage of different ions; and their permeability is not noticeably changed after the death of the cells by chloroform. But living membranes constructed of specifically differentiated epithelial cells behave differently: their ability to oppose or to facilitate the passage o[illegible] physiological functions devolving upon them. [illegible] the cell, at which time also the permeabi[illegible]

The fact demonstrated by Schücking in the case of the snail, *Aplysia*, that long-continued stimulation of the dermal musculature can more than compensate the effects of osmotic pressure, and the discoveries on absorption from the alimentary canal (cf. Chapter VIII), together with the facts summarized above, go to show that *the osmotic processes cannot be the only factors at work in the absorption of substances by animal cells.* The outer limiting membrane of the cell behaves in many respects as a semipermeable membrane, but, so far as we can grasp the matter at present, it appears to differ in many respects from such a membrane. Just as the cell itself regulates the extent of the oxidation processes taking place within it or inaugurated by it, so within certain limits, and independently of the quantitive composition and the osmotic pressure of the surrounding medium, it regulates its absorption and elimination of substance. It is possible that this is due to the specific affinities of the living bodies which constitute the protoplasm. Just as gelatin plates and agar plates take up substances from solution, whether the solution is isotonic, hypotonic, or hypertonic, until their affinity for the substance is satisfied, so the living substance might take up or give off substances according to its affinities, independently of the osmotic pressure. Just what weight this hypothesis, developed by Friedländer and Durig, may have we cannot say definitely at present.

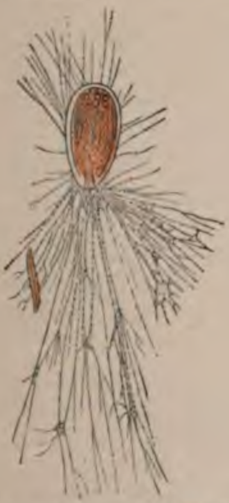

FIG. 19.—*Gromia oviformis*, after Max Schultze. Some of the pseudopodia have caught a diatom, which by gradual shortening of the contractile threads will be taken into the interior of the organism. 20/1.

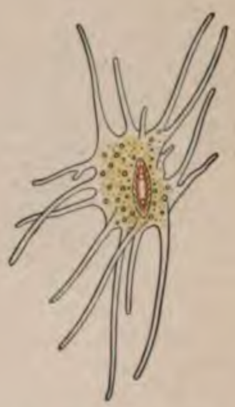

FIG. 20.—*Amœba polypodia*, after Max Schultze. A small organism has been engulfed. 330/1.

In connection with the investigations here discussed opportunity has often been afforded to determine the osmotic tension inside animal cells. It is found correspond to a NaCl solution of 0.7 to 0.9 per cent, and amounts to about 6.5 atmospheres. In order that the aqueous content of animal cells may reserved, it is necessary therefore that the surrounding medium have a ponding osmotic pressure.

Since NaCl plays the most important rôle in maintaining this pressure, one might suppose that this is the only special physiological significance of common salt. That is not the case however, as appears from the fact that a frog's muscle which remains excitable for a long time in a 0.6-per-cent NaCl solution very soon loses its excitability in an isotonic solution of cane sugar (Overton).

2. Naked elementary organisms have the power also *of ingesting solid particles.* In many cases this takes place in a very simple manner. The elementary organism puts out processes, pseudopodia, which apply themselves to the particles of food, then gradually flow around it until it comes to lie

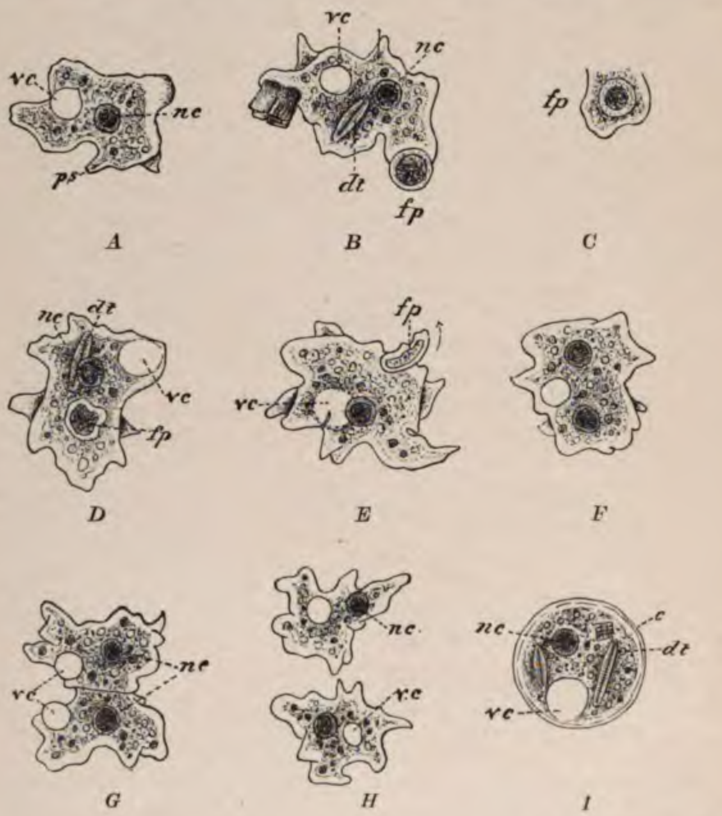

FIG. 21.—*A–H*, Several successive phases in the life history of an *Amœba*, kept under constant observation for three days; *I*, another individual encysted.

A, locomotor phase: the ectoplasm is seen extending to form a pseudopodium, into which the endoplasm passes; *B*, a stage in the ingestive phase; *fp*, a vegetable organism being ingested; *C*, a portion of the *Amœba* represented in *b*, after complete ingestion of the food-particle; *D*, *E*, successive stages in the assimilative and excretory processes; *F*, *G*, *H*, successive stages in the reproductive process of the same individual. It will be noticed (*F*) that the nucleus divides first; *vc*, contractile vacuole; *nc*, nucleus; *ps*, pseudopodium; *dt*, diatom; *fp*, food particle.

within the protoplasm. Examples of this are found in the Amœbæ and other Rhizopoda (Figs. 19 to 23), and in the leucocytes of all classes of animals, which very closely resemble Amœbæ with respect to their structure.

This ability of the leucocytes is of great importance to the body as a whole, for wherever a destruction of tissues takes place either from normal or pathological causes, the *débris* is taken up by the leucocytes and is removed. The leucocytes play an important rôle also in disposing of the pathogenic Bacteria which find their way into the body, since they are able to eat and to digest such organisms (Fig. 22), and thereby to afford the body substantial protection against infection (Metschnikoff).

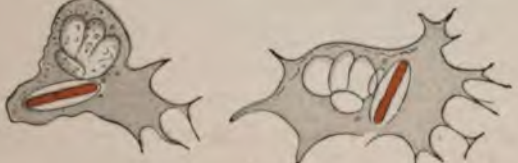

FIG. 22.—A white blood corpuscle of the frog, containing an anthrax bacillus. The two figures were drawn from the same cell at different times, after Metschnikoff.

The more highly organized elementary organisms provided with cilia and a cell mouth, such as the *ciliate Infusoria* (Figs. 24 and 28), ingest solid particles by creating with their cilia a vortex so directed that the particles are driven into the mouth. In this and other similar ways of taking up solid particles the organism can exercise an actual choice of nourishment; certain Rhizopoda for example eat only certain alga cells (cf. Fig. 23).

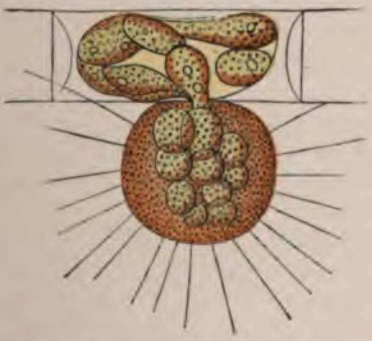

FIG. 23.—*Vampyrella spirogyræ*, a rhizopodous unicellular organism, ingesting the contents of an alga cell, after Cienkowski.

C. DIGESTION

The solids taken up in this way by the cells must undergo various changes in order that they may be of use to the cell. Often this is true also with the dissolved foods. All such processes by which the foods are changed so that they may be assimilated or further elaborated by the cell are included under the term *digestion.*

The digestion accomplished by the cell is either *extra- or intracellular.* In the former case digestion takes place under the influence of special substances, the *enzymes,* formed by the cell. These substances, like catalytic agents, have the property when present in very small quantity of producing chemical changes in great quantities of complex molecules, thereby splitting them into simpler compounds, which in their turn reduce the activity of the enzymes. By the action of enzymes proteid is split into albumoses and peptones, starch into sugar, and fat into glycerin and free fatty acids (cf. Chapter VII). It should be noted further that every special enzyme acts only upon a definite compound or group of compounds. The proteid-splitting enzyme therefore does not act upon starch, nor the starch-splitting enzyme on fats, etc.

It is quite possible that the enzymes can produce their effects inside the cell just as well as in the surrounding medium, and it is very doubtful whether an intracellular digestion takes place anywhere without the help of enzymes, though such participation cannot be definitely asserted.

Enzymes which have the property of dissolving proteids just like the corresponding enzymes in the digestive fluids have been obtained from finely minced organs—spleen, lymph glands, kidneys, liver, heart, etc. It is assumed that they are present in the living cells, though this has not been finally proved. Nothing definite can be said at this time with regard to the importance of such enzymes in the normal processes of the body. It is possible that in starvation they may effect the solution of the tissue proteids, also that the autolytic processes which take place after death are initiated and carried on by such enzymes.

The *enzymes are products of cell activity,* but once they are formed they act entirely without the help of the cell and are nonliving substances. In general it is supposed that they are proteid in nature, and in fact Pekelharing has prepared from the stomach of the dog a very pure enzyme (pepsin) which was free of phosphorus and had the constitution of proteid. But it would be premature to draw any general conclusions from a single observation.

Enzymes occur in the cells for the most part in the form of precursors, known as *zymogens.* Often the zymogen is changed into the active enzyme in the act of secretion; or its *activation* may be brought about under the influence of another enzyme.

Enzymes are only slightly diffusible, but they pass through a porcelain filter and can be separated in this way from the cell fragments of an extract or juice. In the dissolved state they withstand heating up to 70° C.; in the dry state many enzymes are not destroyed by a temperature of over 100° C. In general they are most powerfully active at 35° to 45° C.; at a lower temperature they act more feebly, but if warmed again will regain their activity even after having been reduced to a temperature as low as – 192° C. They are destroyed by mineral acids and alkalies of sufficient strength. With some enzymes also the decomposition products formed by them exert an inhibiting influence on their further activity. On the other hand their activity is but slightly affected by the protoplasmic poisons.

Various facts favor the view that enzymes exercise their specific effects only after uniting with the substance acted upon. Thus pepsin for example unites with the proteid fibrin so firmly that it cannot be removed by washing with water. The fact also that when mixed with the appropriate substances enzymes endure a higher temperature than otherwise gives a certain support to this conception.

Recently Croft Hill has shown that the enzyme formed in the yeast cell by which maltose is changed into dextrose, has the power in concentrated solutions of sugar (over four per cent) of changing dextrose back into maltose; that what takes place is therefore a *reversible process.* Similar phenomena have since been observed with other enzymes. Pancreas extract effects a partial synthesis of ethyl butyrate from ethyl alcohol and butyric acid (Kastle and Loevenhart). By means of a lactose-splitting enzyme E. Fischer and Armstrong prepared isolactose from galactose and glucose in equal quantities, etc.

It is very probable that this reversibility of enzyme action is of very great importance in the transformations taking place in the body, although we are not yet able to foresee its entire range.

D. THE OXIDATIVE PROCESSES

Attempts have been made to give an exhaustive theoretical explanation of the oxidative processes going on in the tissues, and several hypotheses have been put forward. Some of these suppose that the influence of the animal tissues on the physiological oxidations consists of an increase in the oxidizing activity of oxygen; some assume that the tissues in mediating oxidations do not influence the oxygen itself, but act on the oxidizable substances making them more accessible to the oxygen.

We cannot here enter into the development of these theories since, as they stand to-day, they are not by any means able to explain the facts. We may say only that from both fresh and dead organs hardened in alcohol, it is possible to extract with water a substance which oxidizes certain substances like benzyl alcohol, salicyl aldehyde and glucose (Jacquet). According to Spitzer this substance is an iron-containing nucleo-proteid derived from the nucleus. Whether it has any special significance in the physiological processes of the cell cannot be said definitely as yet, because of the possibility that it is set free only by the destruction of tissue elements. That in any case its physiological importance is only secondary, would appear to be sufficiently shown by the fact that its quantity, or more correctly, its oxidizing function as determined in the manner above mentioned is considerably greater in the glandular organs (spleen, liver, thyroid, kidneys, etc.) than in the muscles, where combustion takes place most extensively.

The following discoveries appear to afford a wider outlook. In the *alcoholic fermentation* effected by the yeast plant, maltose dissolved in water is changed under the influence of an enzyme formed by the yeast cells into grape sugar, and this is split into carbon dioxide and alcohol. Until recently it was supposed that the latter cleavage could only be accomplished by the vital activity of the yeast cells themselves, which appeared in fact to follow from a number of experiments. By trituration of the yeast cells and subsequent compression with a pressure of 400–500 atmospheres, however, E. Buchner (1897) succeeded in obtaining a sap, which after being filtered through sterilized "infusorial earth" and thus being freed entirely of yeast cells, was still able to split sugar into alcohol and carbon dioxide. The active substance contained in the sap Buchner named *zymaze.*

This discovery opens up new prospects for our whole conception of the mode of decomposition in the animal body. It makes possible the assumption that not only the yeast cell but all other cells carry out the chemical work characteristic of their vital activities by means of substances analogous to the enzymes and capable of being isolated which are formed within the cells and are given off by them. It would be premature however from the present standpoint of science to make such a generalization even hypothetically. For the substances formed in the processes under consideration are so manifold, and the essence of the processes is still so obscure that immediate dissimilation effected by the vital activity of the cells cannot without further information on the subject be completely excluded. Moreover, the oxidation processes of the body are so well regulated in relation to the amount of work to be done and the time of doing it, that it is difficult to imagine how they could be brought about exclusively by ferment action.

Any dissimilation accomplished by the direct action of the cell, in contradistinction to the effect of the enzymes and zymaze, is designated as *ferment action,* and the cells participating are known as *organized ferments.* Substances resulting from such action represent decomposition products formed directly by the vital activity of the cell. Carbon dioxide which is produced in every living being belongs (at least in part) in this category, as do other substances which especially characterize the different organisms, e. g., the peculiar metabolic products of different Bacteria (*toxins*).

It is generally true for all cells that the substances produced in their metabolism are harmful to the organisms themselves, and if retained in large quantities they are fatal. Hence neither yeast cells nor Bacteria can live continuously in the same solution, even though there is no lack of nourishment, unless provision is made for the removal of the products of decomposition from the solution.

E. THE ELIMINATION OF DECOMPOSITION PRODUCTS

The cells of course cannot remove the waste products from the medium in which they live. They can do no more than remove the products from their own bodies. The indigestible residues of the solid food such as walls of Algæ, cases of diatoms, the chitin of rotifers, etc., are egested from the free-living cell body in a manner exactly the reverse of their ingestion. The remnant is brought to the surface of the cell, the protoplasm gives way in this particular place, the body to be eliminated is extruded, and the cell withdraws from it.

The gaseous excretions, carbon dioxide and oxygen, are probably eliminated according to the laws of diffusion (cf. Chapter IX).

We have as yet but little reliable information as to *how dissolved substances leave the cell.* To reason by analogy with the manner of their absorption we ought to find at work besides the osmotic processes, an active influence on the part of the cell itself. If the products cannot be removed immediately they are sometimes rendered harmless by a combination of some sort. For example, oxalic acid, which is poisonous, is bound up with calcium in the insoluble and therefore harmless compound calcium oxalate. In Chapter XIII we shall discuss a number of analogous processes in the higher animals. A highly specialized mode of removing fluid waste from the body of an Infusorian is shown in Fig. 24.

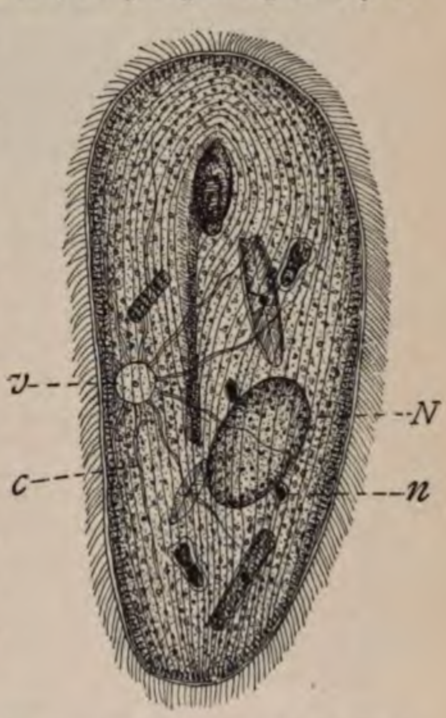

FIG. 24.—*Frontana leucas*, after Schewiakoff. *N*, macronucleus; *n*, micronucleus; *c*, one of several excretory canals leading into the excretory vacuole; *v*, by contraction of which the fluid contents are ejected. Several ingested diatoms are to be seen.

F. SECRETION

In unicellular as well as in multicellular organisms, though in the latter probably to a much greater extent, the cells by their own activity form various substances which either serve the purposes of the cell itself, or, in the multicellular forms, are essential to the purposes of the entire body. We include all such substances under the head of *Secretions.*

To the secretions belong the enzymes and analogous compounds, such as the products of the so-called internal secretions (cf. Chapter XI), also most of the skeletal substances, as the chitinous cases of insects, the calcareous shells of Foraminifera, the cell membranes, etc.; and, finally, the intercellular substances such as occur in the fibrillar connective tissue, cartilage and bone. How far these substances arise by transformation of the living protoplasm, or are only produced by its activity cannot be regarded as settled. But it is probable that the latter alternative holds in the case of those structures which are formed of silicic acid or calcium carbonate or phosphate; for it can scarcely be supposed that structures of this kind arise directly from protoplasm.

G. MOTILITY

It has already been necessary to refer briefly to the movements of the elementary organisms, but since motility is one of the most important functions of living substance, we must study it here in its different manifestations.

1. *The protoplasm of a plant cell inclosed within the membrane* exhibits different forms of motility. Some of these, as for example the migration of chlorophyll bodies, take place very slowly (Fig. 25). In diffuse daylight the *chlorophyll bodies* are so placed that they present their greatest surface to the light (T); in direct sunlight they are so placed that their narrow edge is turned toward the incident rays (S); while in windows a third position (N) may be taken. The purpose of these movements is doubtless to protect the plant in strong illumination from a too intense effect of the light, and in moderate illumination to secure the plant as great an effect as possible.

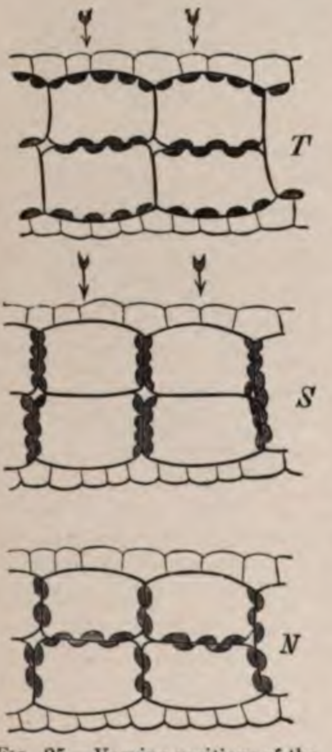

Fig. 25.—Varying positions of the chlorophyll bodies in the cells of *Lemna triscula*, according to the direction of the incident light rays, after Stahl.

We observe in plant cells also *streamings of protoplasm* which can be followed by the migration of the granules. In these movements the protoplasmic particles either flow in different directions, often in great confusion (circulation), or the protoplasm collected along the wall is caught in a rotatory movement all in the same direction, in which the nucleus and often the chlorophyll bodies are dragged along (rotation) (Fig. 16).

2. The simplest kind of protoplasmic movement *in the naked cells proceeds in a manner similar to that just mentioned*, as may be observed in the Amœbæ (Figs. 20, 21, 26), and in the leucocytes of multicellular animals (Figs. 22, 27). During rest the *Amœba* is spherical. When it begins to move one or more processes protrude from the periphery of its body. By a kind of *streaming movement* the protoplasm of the cell body then flows into this process or processes and the position of the entire mass of the animalcule is thereby changed. The protrusions are not preformed structures, for the cell has the power to put out such a process from any point of its surface and to withdraw it again. It is on account of their transitory character that they are called *pseudopodia*, or false feet.

The appearance of the pseudopodia in different species of elementary organisms is very different. In unicellular animals provided with an external skeleton they are modified according to the character of the openings in the skeleton through which they protrude (cf. e. g., Fig. 14). We meet with short and thick, or long and slender, threadlike or thorn-shaped pseudopodia; or again with those which project quite independently of each other, or which unite in the most complex sort of a network (Figs. 19, 20, 21, 26).

Both phases of the movement of pseudopodia in *Amœba*, namely *expansion* and *contraction*, are to be regarded as active processes, and the two are of equal importance in ingesting food or in locomotion. In other kinds of movement the most important phase consists in a reduction of the surface of the cell—i. e., in contraction. To this category belong especially the movements of the smooth and cross-striated muscles, to which we shall devote proper attention in Chapter XV.

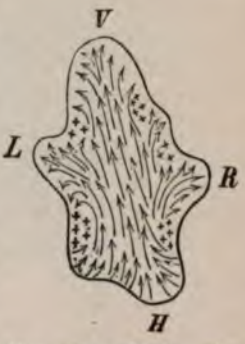

FIG. 26. — Mode of movement of an *Amœba*. The arrows indicate the direction and strength of the protoplasmic currents; the crosses, the resting places. For the instant the principal line of movement is from *H* toward *V*, but at any other moment it may turn toward *L* or *R*.

3. The cell body of certain unicellular organisms presents specially differentiated contractile elements. *Stentor*, for example, has in its outer sheath of protoplasm smooth muscle fibrils running almost parallel; *Vorticella* (Fig. 28) contains only a single smooth muscle fiber composed of several fibrils. This leaves the body as a thick cord, and is surrounded by an elastic membrane to the inner side of which it adheres along a spiral course from one end to the other. It serves as a stalk for the attachment of the organism. If these contractile fibers are roused to activity, they become shorter and thicker just like true muscles, and thereby change the form of the cell in a corresponding way.

4. In numerous unicellular organisms and in numerous cells of multicellular organisms, we find *cilia* or *flagella* as special differentiations of the cell body. These are not temporary like pseudopodia, but permanent structures of greater or less length attached to the outer surface of the cell. They are in constant motion and occur on every cell or on a great majority of the cells forming a ciliated surface. If the cell bears only a few (1 to 4) such structures, they are called flagella; if a larger number, they are called cilia. In certain organisms they can be counted by the hundreds and thousands.

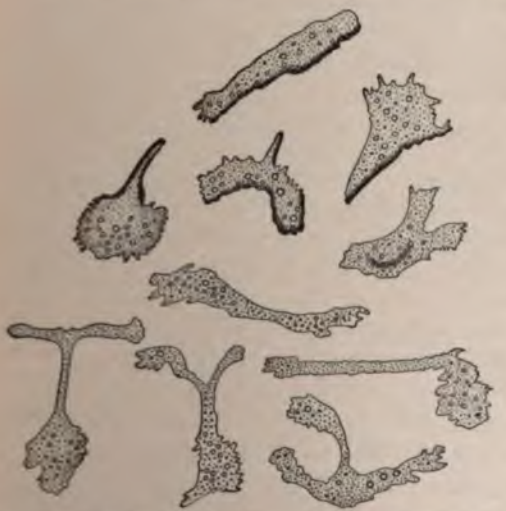

FIG. 27.—White blood corpuscles at 38° performing amœboid movements, after Max Schultze. The different figures are all drawn from the same corpuscle.

Flagella are affixed either to the anterior or the posterior end of the cell body. The former arrangement is found in the Flagellata, in the spermatozoids of plants, many Bacteria, and in the swarm spores of many Algæ and Fungi. In locomotion the flagella precede and pull the body after them. The latter arrangement is found in the spermatozoa of most animals, where the flagellum drives the cell body forward after the manner of a propeller.

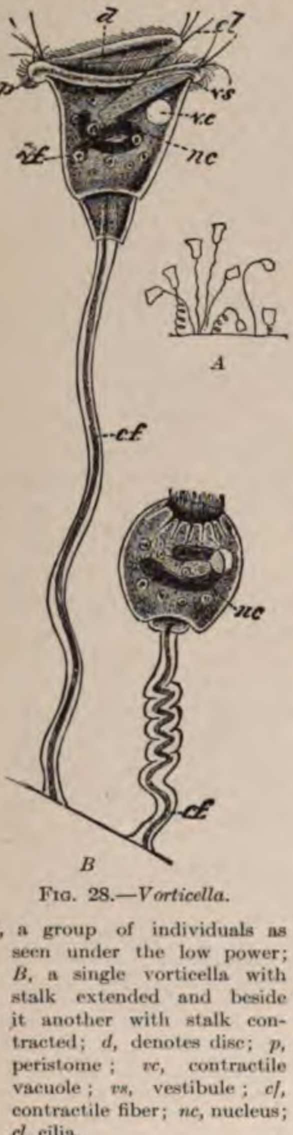

Fig. 28.—*Vorticella.*

A, a group of individuals as seen under the low power; *B*, a single vorticella with stalk extended and beside it another with stalk contracted; *d*, denotes disc; *p*, peristome; *vc*, contractile vacuole; *vs*, vestibule; *cf*, contractile fiber; *nc*, nucleus; *cl*, cilia.

If the cilia should beat back and forth in both directions with equal force, only a to-and-fro movement would result, and no locomotion would be possible. Careful investigation of both flagella and cilia has shown that they always strike more forcibly in one direction than in the other, a fact which at once makes clear the mechanical results of their movements.

In the freely motile cells the object accomplished by the ciliary movement is locomotion. In addition to this, if the cell is swimming in a fluid specifically lighter than itself, motion of the cilia prevents it from sinking to the bottom. Again in certain unicellular animals they participate in the ingestion of food, being arranged in a circle around the mouth, and when in motion creating a vortex in the water which sucks suspended particles into the mouth (Fig. 28).

The ciliated cells covering the surface of the mucous membranes in Metazoa drive such particles as may happen to be on the surface in a given direction, and thus play a rôle in many ways very important to the animal.

Cilia are always fastened to a protoplasmic substratum and are never outgrowths of a firm cell membrane. Very often, however, they are not immediate extensions of the protoplasm, but rest directly upon a thin layer of transparent substance which, though very closely resembling the substance of the cilia, appears not to be contractile but to lie as a kind of coat on the naked surface of the cell protoplasm. The coats of the adjacent cells are so closely connected that in many cases a considerable patch of this layer can be lifted up as one piece.

Certain cilia continue to move even if they be separated entirely from the protoplasm or the basal part of the cell. Since both cilia and flagella can of themselves perform many complicated movements we must assume that they *consist of a contractile substance.* If in addition we assume that they contain also a noncontractile supporting substance, we should have a somewhat satisfactory explanation of the different forms of movement of these structures (Pütter).

In most cases ciliary movement is not influenced in any manner by the adjacent or by the distant cells, and in the mucous membranes of the vertebrates it appears to be entirely *independent of nerves;* for ciliated cells continue to move after they are cut out of the body, and in the human body for as much as three days after death (Valentin). Hence it is the more remarkable that in a row of cells the cilia always move in complete harmony even if the cilia are not in contact with each other. This and the further fact that a stimulus, applied to a portion of the epithelium where ciliary motion has ceased, can be transmitted to a portion where it is still active, go to show that the basal part of the cell must have something to do with the regulation of ciliary movements. Nevertheless much here remains to be explained.

5. Still other forms of movement than those already discussed occur in the animate world. The following may be briefly mentioned. Various unicellular animals (Radiolaria, Rhizopoda) can raise or lower themselves in the water where they live *by changes in their specific gravity.* Arcellæ and Difflugiæ rise by developing a bubble of carbon dioxide in their cell body. *Thalassicola* (Fig. 15) swims at the surface of the sea because its vacuoles contain a fluid specifically lighter than sea water. Under certain conditions it can sink itself by rupturing the sheaths of the vacuoles which then fuse together. When the vacuoles are reformed the animalcule once more mounts upward. Finally, in plants a great many movements occur through *swelling of the cell wall,* and through *changes of turgor,* which we cannot discuss in this book.

H. PRODUCTION OF LIGHT

Certain putrefactive Bacteria which live on decaying flesh of marine fishes and on meat, as well as certain Fungi and a few insects have the power of producing light. In certain places where the sea water glows it is found on filtration that the glowing substance remains on the filter and is not found in the filtrate; the cause of the light is therefore an insoluble substance. Microscopical examination of the residue on the filter reveals millions of phosphorescent organisms belonging to all classes of the invertebrates.

That the phosphorescence of these animals is not due to previous exposure to the sun's rays follows from the fact that even when they are kept for a long time in complete darkness, they glow just as strongly as their companions which have been in the sunlight. The phosphorescence ceases however when the animals are brought into a medium unsuitable for respiration; it therefore represents a true oxidation process.

Closer investigation of this phenomenon proves that it is initiated by the *activity of the living protoplasm*, for the organisms produce light only so long as they are alive. In the case of *Pholas* (a mussel), the phosphorescent substance can be thrown out of the body, but it is formed only by the activity of the living protoplasm. The phosphorescence arises through the action of a special enzyme on this substance (R. Dubois). In the "lightning bug," *Lampyris*, nerve fibers have been demonstrated running to the light-producing organ. The animal suppresses its light when there is a noise; the darkening then begins at the proximal end and spreads to the distal end of the organ. It is worthy of note also that the light produced by the "lightning bug" is deficient at both ends of the spectrum. We have here in other words a source of light which is devoid or almost devoid of the ultra-red and ultraviolet rays (Langley and Very).

I. FORMATION OF HEAT

Heat is formed in all dissimilative processes, and since processes of this kind occur everywhere in animate nature, we may say that the *generation of heat is universal.* This cannot always be demonstrated; for in the isolated elementary organisms the quantity formed is so small that it cannot be measured with our instruments. In plants as a rule heat is formed so slowly that as fast as it is generated, it is radiated to the surrounding medium; consequently the temperature of the plant cannot be elevated perceptibly above the medium. It should be said also that the abundant transpiration occurring in plants has much to do with keeping down their temperature. The same is true and for the same reason in most of the so-called *cold-blooded* or *poikilothermos* animals, that is, animals in which the body temperature rises and falls with the temperature of the surrounding medium. In dry air, on account of evaporation from the surface of the body, the temperature of a cold-blooded animal is usually lower than that of its medium. In a moist or water-saturated atmosphere the body temperature may rise some tenths of a degree. This is true likewise of cold-blooded animals which live in water. Only in the so-called *warm-blooded* or, more correctly, *homoiothermos* animals (birds and mammals)—i. e., animals whose body temperature remains constant in spite of the variations of the surrounding temperature—can the production of heat be demonstrated directly and without difficulty. In these animals the temperature of the body is almost always higher than that of the medium in which they live.

Under certain circumstances it can be shown very clearly that in plants as well as in cold-blooded animals heat is actually formed. With peas which have been allowed to germinate in a funnel under a bell jar a rise in the temperature of 1.5° C. has been observed. In the spadix of the Araceæ (e. g., "skunk-cabbage") a temperature of 15° C. higher than that of its surroundings has often been witnessed. Likewise in the fermentation of sugar solutions by the yeast plant elevations of temperature of about the same extent may occur.

With regard to the body temperature of the *cold-blooded* animals, the following data on the excess of the animal's temperature over that of its surroundings have been gathered: various invertebrates in water 0.21°–0.60 C.; earthworms in a glass vessel 1.4° C.; bees in a beehive 21° C.; moving butterflies 14° C.

The animal heat of warm-blooded animals will be more fully discussed in Chapter XIV.

J. GENERATION OF ELECTRICITY

The enormous number of investigations on animal electricity begins—if we except the electrical fishes—with the pregnant observation of Galvani that *a frog's thigh contracts* when it is touched in two places with the ends of a metallic arc (September 20, 1786). From this observation Galvani thought himself justified in concluding that animals have a peculiar kind of electricity and that it is of very great importance in the functions of the animal body; in fact, physiologists of that time thought their dream of a vital force was at last to be realized.

It was reserved for the discriminating insight of Volta to show that these contractions are conditioned upon the dissimilarity of the two ends of the metal touching the moist conductor, and upon the production thereby of a galvanic arc. Further investigation proved, however, that *electrical differences of potential* do occur in the animal body. The events historically most important from this point of view are: the discovery of the so-called frog current—i. e., of a current running from the feet to the head of the frog (Nobili, 1827); the demonstration that the isolated muscle under definite circumstances gives a regular current (Matteuci and Du Bois-Reymond, 1840–1843); the discovery of the electrical variations in muscular activity (Matteuci and Du Bois-Reymond, 1842); and the discovery of the nerve current and its variations (Du Bois-Reymond, 1843).

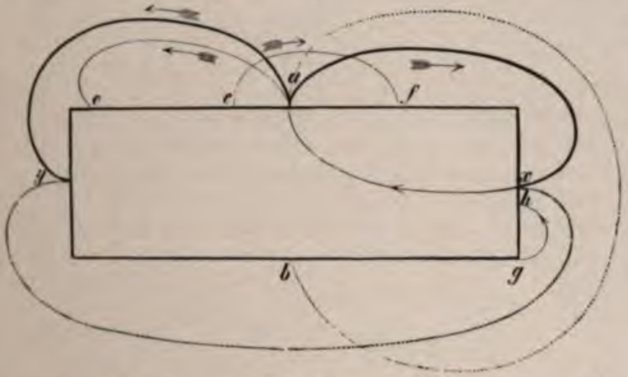

FIG. 29.—Schema representing the current of injury, or demarcation current, in a muscle, after Foster.

The object most used in these investigations is cross-striated muscle. If two points of an exsected muscle be connected with a galvanometer an excursion of the needle nearly always occurs; between the two points of the muscle there is, therefore, a difference in tension. More detailed study has shown that these tension differences are perfectly regular, and in muscles with parallel fibers they have been found to take the following form (Du Bois-Reymond) (cf. the schema in Fig. 29). If a longitudinal surface and a transversely cut surface of such a muscle be connected with a galvanometer, a current is obtained, which in the muscle is directed from the transverse to the longitudinal surface, and which reaches its greatest intensity (0.06 to 0.08 volt) if the leading-off electrodes are placed in the middle of the two surfaces. If two asymmetrical points of the longitudinal surface be led off weaker currents are obtained, which in the muscle are directed from the periphery toward the middle. With two asymmetrical points of the cross section a current is obtained which passes from the middle toward the periphery. Finally, if symmetrical points of the cross section or of the longitudinal surface be connected, no differences of tension are shown (Fig. 29, dotted lines). From these facts it follows that *the entire longitudinal surface of the muscle possesses a positive tension, every cross section a negative tension.*

It has been shown by Hermann (1867) that in an entirely uninjured, resting muscle there are no such differences of tension. If the skin be removed very carefully from the gastrocnemius of a frog and great pains be taken that it does not come in contact with the secretion of the skin, no current at all, or only the very weakest one, is obtained when the muscle is connected with the galvanometer. If on the other hand the muscle be injured in any way in the neighborhood of one electrode, a strong current appears. The uninjured, resting heart also gives no current (Engelmann).

These and other discoveries—among which should be mentioned the fact that the current of injury does not appear in its full strength immediately but develops gradually—induced Hermann to propound the following theory in explanation of the current of rest, which at this time is the one most acceptable to physiologists. The cause of the difference of electrical tension in the resting muscle lies in the injury which it receives. In a partially injured muscle every point of the injured portion is negative to every point of the uninjured part. The facts may be expressed in the following general proposition: *in every injured muscle fiber the demarcation surface between the living and the dead contents of the fiber is the seat of an electromotive force directed toward the living part.* On this account Hermann designated the current of rest as the *demarcation current.*

Exactly the same electrical phenomena as in the resting muscle appear in resting nerve.

Electrical currents appear also when a muscle or a nerve is active, and these currents are intimately connected with the functional condition of the tissue. The general law of these currents (*action currents*) may be comprehended in the following statement: *Every active portion of muscle or of nerve maintains a negative relation toward the resting part* (Bernstein, 1867). We can therefore condense the law for the rest current and the action current into the following simple formulation: *In muscle and in nerve every active or injured part maintains a negative electrical relation toward every other part which at that time is at rest or is uninjured.*

Further study of the action current will be postponed to the discussion of the general physiology of muscles and nerves (Chapter XV).

We meet with analogous electrical phenomena in many other tissues. The currents present in glands are of special interest. Du Bois-Reymond proved that the skin of the Amphibia is *the seat of a current directed from without inward* which he ascribed to the secretion of the skin peculiar to these animals. Later investigations have made us acquainted with similar currents in many other objects (mucous membrane of the frog's tongue, of the pharynx and cloaca of the frog, skin of the Amphibia and fishes, and of the leech, etc.), and have shown that they are generated by the mucus-forming epithelia composed of single-celled glands, as well as by other epithelia not glandular (Reid). Both the strength and the direction of the current of action may be modified by such agencies as pilocarpine, which stimulates secretion, by excitation of the mucosa or of the glandular nerves, by changes of temperature, of the blood supply and of the water content.

We find similar skin currents in all Mammalia including man. If the two hands or the two feet of a man be led off symmetrically to the galvanometer and one arm or one foot be moved voluntarily the needle makes an excursion, which is not caused by the muscular contraction in itself but by the process of secretion going on at the same time in the sweat glands of the contracted extremity. This current passes from the outside to the inside of the skin. A very similar skin current has been observed in the sweating of different mammals.

Biedermann observes that one cannot draw a sharp line of separation between current of rest and current of action in epithelial and glandular cells, for the reason that the differences of tension met with are always the expression of differences in the chemical relations of the neighboring parts. From this point of view it appears quite arbitrary, or incorrect indeed, to speak of the current of rest in contradistinction to the current of action of a glandular structure, since in both cases one deals with the effects of certain metabolic processes going on in definite parts of the cell body, which by direct or indirect stimulation are only changed in one direction or another. It is better, therefore, to say that the ordinary skin current is produced by the negativity of that portion of the cell which is being transformed into mucus, toward the protoplasmic portion (Hermann).

As above remarked, this inwardly directed current may, under certain circumstances, undergo a complete reversal. To explain this we can make only one assumption, namely, that the same epithelial cell has the power to act electrically sometimes in one sense, sometimes in the other. This is borne out by the fact that each cell is the seat of two different chemical processes (assimilation and dissimilation), which, going on at the same time, give rise to opposite tensions. The deviation occasionally observed would, according to this, always be the resultant of the two antagonistic forces (Hering, Biedermann).

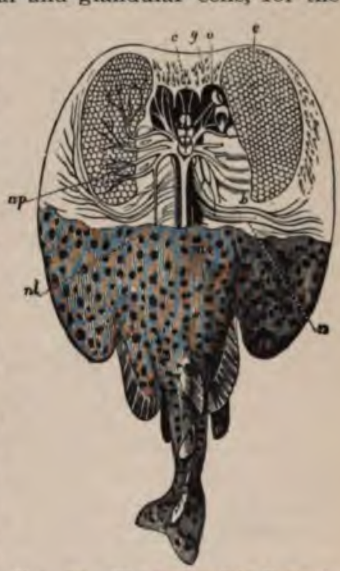

Fig. 30.—The cramp fish, *Torpedo*, dissected to show electric apparatus, after Huxley; *b*, gills; *c*, brain; *e*, electric organ; *g*, cranium; *me*, spinal cord; *np*, branches of pneumogastric nerves to electric organs; *o*, eye.

It is possible that a relationship similar to this exists between the chemical processes underlying the secretion of water on the one hand and the secretion of organically specific constituents on the other (Biedermann). Perhaps from this point of view are to be explained certain results obtained with the digestive glands, of which more in Chapter VII.

Electrical currents have been demonstrated even in plants, where, just as in the animal tissues, an injured place is found to be electro-negative to an uninjured place. Electrical effects appear also under appropriate circumstances in certain parts of plants which are entirely uninjured. Thus, differences of tension are obtained between cells or cell territories of an organ or of a whole plant which maintain different chemical relations to each other.

For example, according to Waller, the processes taking place in the formation of starch are bound up with electromotive phenomena. If a shaded and an exposed part of a green leaf (Fig. 17) be connected with a galvanometer, when the light falls on the exposed part, an electric current is observed which runs in the leaf itself from the insolated to the shaded part. The deflection begins after some three to ten seconds and lasts as long as the illumination continues, if that time does not amount to more than about five minutes. The effect is least in diffuse daylight, greatest in direct sunlight and is abolished by boiling the leaves. All such effects are absent in flower parts devoid of chlorophyll.

Whether these electrical variations have any general significance for the cells exhibiting them, or for the individuals containing the cells we cannot say definitely. But the matter is clearer in the case of the well-known electric fishes, of which there are many different species. In most of these fishes the electrical organs are metamorphosed muscles, but in *Malapterurus* it represents a transformation of the glands of the skin. In rest the organ shows no current; but under the influence of the specific nerves, as well as by direct stimulation it develops very strong electric currents, the force of which in the cramp fish (Fig. 30) amounts to thirty-one volts. That such currents must be of great service for these animals in their struggle for existence is at once perfectly obvious.

§ 3. THE EFFECT OF EXTERNAL INFLUENCES ON CELLS

A. ON STIMULI IN GENERAL

The fundamental property to which we trace the total activity of the living substance is its *irritability*—i. e., its ability under the influence of all kinds of agents to change its metabolism, and therefore to change its transformation of energy, in one direction or another. All those agents which have the power to evoke a change of this kind are called *stimuli*. Among them are to be included different chemical reagents, mechanical agents of all kinds, heat, light and electricity.

The change in metabolism produced by a stimulus is either dissimilative or assimilative (cf. *supra* page 22). In the former there is a production of *kinetic energy* and the process taking place in the cell is described as an *excitation*. In the latter we have a storing of potential energy, and the change is often described as a *trophic* effect. The stimulus may however check metabolism for a longer or shorter time, may bring it to a standstill momentarily, or stop it altogether. We speak then of a *paralysis* of the cell. Paralysis represents a negative condition with respect either to the assimilative or the dissimilative responses.

By stimulation of certain nerves the dissimilative action of the innervated organ may be abolished. Of such phenomena, described as *inhibition*, the influence of the vagus on the heart has been most closely studied. When the vagus is stimulated artificially the heart beats more slowly, and with a stimulus strong enough it stops in diastole (the brothers Weber, 1846). This inhibition is not a kind of paralysis, for phenomena to be described later (Chapter VI) show that while the heart in vagus standstill is inexcitable, it is not paralyzed.

The assimilative and dissimilative processes often go on side by side in the same cell. Since the latter are best known it will be well to discuss them first. We shall make five general observations, which apply to all dissimilative processes.

1. The production of energy is many times as great as the energy of the stimulus employed, which will appear for example in the following experiment: A frog's gastrocnemius is fastened in a clamp by the femur and a weight of 48.5 gm. is suspended from its lower end. The nerve attached to the muscle is laid upon a solid block. If now a weight of 0.485 gm. be allowed to fall upon the nerve from a height of 10.1 mm. the muscle contracts and lifts the weight 3.8 mm. high. The work done by the muscle is $48.5 \times 3.8 = 184.3$ gm. mm.; while the active force of the stimulus is equivalent to only $0.485 \times 10.1 = 4.9$ gm. mm. of work. The mechanical work of the muscle called forth is therefore about thirty-eight times the active force of the stimulus, taking no account of the heat developed by the muscle at the same time.

All other cells conduct themselves just like the muscle cells in this experiment, when they develop energy through dissimilative processes. We meet with numerous analogies also in inanimate nature. For example, a weight of 10 kg. suspended by a cord 10 m. above the floor, represents a potential energy of 100 kg. m. In order to change this potential energy to kinetic we have only to cut the cord, which of course does not call for an effort of 100 kg. m. The same is true when powder is exploded by a match, etc.

In all such cases we speak of energy having been *liberated*, a term which conveys to our minds the idea of an impetus by which a transformation from potential to kinetic energy is produced, where in the nature of the case the size of the impetus need be only very insignificant.

2. Generally speaking, in order to call forth a demonstrable effect in living substance, the stimulus is effective only from a certain minimum onward. If the stimulus is increased above this by uniform increments, the response usually increases, but the increase becomes less the stronger the total stimulus, until finally the maximum response is reached, beyond which it cannot rise however much the stimulus is strengthened.

3. Another property characteristic of the behavior of living protoplasm, which is developed to different degrees in different cells, is its power *to summate the effects of stimuli.* If a loaded muscle be affected by a maximal stimulus, it contracts to a certain extent; but if it be affected by another stimulus before this contraction ceases, it contracts still further. With a sufficiently rapid succession of stimuli contractions may be obtained which are very much stronger than that obtained by a single stimulus with the same load.

4. All excitation processes are accompanied by the development of heat and electricity. The other forms in which the dissimilative processes manifest themselves differ with different kinds of cells; toward every effective stimulus, *a cell always reacts in a way which is characteristic for its kind.* Thus whatever the stimulus employed, a muscle cell always responds with a contraction; a salivary gland cell, when stimulated, always secretes saliva, etc. In the following discussion of the different stimuli it will not be necessary to enter specifically into the various forms of activity of the different cells.

5. *Those agents which evoke a response as a rule also alter the excitability of the living substance*—i. e., under their influence a given stimulus produces a stronger or weaker response than if it were acting alone. We must therefore make a distinction between *excitation* and the *alterations of excitability* (positive or negative). An excitation may be said to have taken place if a given stimulus can be shown to have started a dissimilative process. If, however, the stimulus produces no effect of this kind, but a second stimulus under the influence of the first produces a response stronger or weaker than it otherwise would, then the first stimulus has increased or diminished the excitability of the cells stimulated. If the stimulus becomes too strong, the functional powers of the living substance may be either reduced or destroyed.

B. AUTOMATIC EXCITATION

When protoplasm is protected from all possible external influences, it still exhibits the functions which we have learned to regard as essential: absorption of food, motility, digestion, heat formation, etc. There must be therefore inside the cell something which calls forth its activities, and from all that is known to us on this subject, we may assume with a high degree of probability, that the excitation is *caused by the products of metabolism formed in the activity of the cell.*

The significance of stimuli arising in the body itself appears from discoveries which have been made concerning the activity of the central nervous system in the higher animals. If for example a rabbit be choked by compression of the trachea, within a short time there appear powerful respiratory movements, convulsions of the whole body musculature, contractions of the vascular walls, etc. In this case the decomposition products normally eliminated in the expired air are retained in the body and bring about the powerful stimulation of the central nervous system in the manner observed (cf. Chapter XXII). Similar phenomena appear when by extirpation of the kidneys the fluid decomposition products otherwise removed from the body by them, are allowed to collect in the body in large quantity.

The direct excitation produced by metabolic products is called *automatic* excitation, because the exciting substances are formed by the activity of the protoplasm itself. That is to say, in this case the cells develop within themselves *the stimuli which rouse them to continued activity.*

C. CHEMICAL STIMULATION

Automatic excitation, as it is here defined, is a kind of *chemical stimulation*, and fundamentally is, so far as we can judge, of exactly the same nature as the excitation which we can produce artificially by various kinds of chemical substances.

Unicellular organisms, Amœbæ and other Rhizopoda, are made to contract by contact with a one- to two-per-cent sodium chloride solution, 0.1-per-cent hydrochloric acid, one-per-cent potassium hydrate or weak solutions of other acids, alkalies and salts; they draw in their pseudopodia and assume a spherical form. The same substances quicken the movements of the flagellated and ciliated cells sometimes in a very high degree. Nerves and muscles of the Metazoa as well as the contractile fibers of the single-celled organisms behave in a similar manner. As regards muscle Hering has shown that various substances which for a long time were supposed to stimulate chemically, in fact stimulate by closing the demarcation current of the muscle. Here belong the so-called physiological salt solution (0.6 per cent), solutions of fixed alkalies up to 0.1 per cent, and different salt solutions. Solutions also, which stimulate chemically, may cause muscular contractions in this way, if they are good conductors. A purely chemical stimulation of the muscle takes place therefore only by means of fluids which do not conduct electricity or do so very poorly, or by means of substances applied only to the uninjured longitudinal surface of the muscle.

As Biedermann has shown, the cross-striated muscles of the frog fall into rhythmical contractions, if they are placed in weak solutions of Na_2HPO_4, Na_2CO_3, Na_2SO_4, NaOH. Loeb has studied these contractions further in the light of the dissociation theory, and has come to the conclusion that they are produced only by certain ions (e. g., Na, Cl, Li, F, Br, I), but are impeded or rendered impossible by others (e. g., Ca, K, Mg, Be, Sr, Co, Mn)—the excitability of the muscle not being changed in either case. Hydroxyl and hydrogen ions hasten the appearance of the contractions without being able directly to call them forth. Solutions which do not contain electrolytes produce no such contractions.

The theoretical significance of these and related facts cannot be discussed here because we cannot yet adequately survey the field recently opened up by these investigations. We may, however, expect from this quarter very valuable results on the chemical relations of the living being in the near future.

Chemical stimuli which have a higher osmotic tension than that of the structures to be stimulated, may exercise an exciting influence or may alter the excitability by the *extraction of water*, as probably occurs in many cases with the nerves.

That this is not the only determining factor however, and that the peculiar properties of the chemical substance exercise an essential influence, appears from the fact *that equimolecular solutions in general stimulate more powerfully the higher the molecular weight* (Grützner). Thus sodium iodide for example stimulates more powerfully than the bromide and chloride, whereas the osmotic tensions of all these is equal.

Besides these direct responses to stimuli and the alterations of excitability, which we must pass over, certain substances exercise a very remarkable influence[1] on the movements of free-living cells *by attracting or repelling them.* These phenomena are designated by the term *chemotaxis* and are described in the one case as positive, in the other as negative. Different substances exercise different influences on various cells, and the same substance in different concentrations may produce different effects on the same organism.

Some examples of chemotaxis may be cited here. Certain forms of Bacteria are attracted by oxygen, and in a microscopical preparation which contains these Bacteria together with some alga cells one may observe how they gather around the alga drawn by the oxygen which is set free by the chlorophyll (Fig. 31, Engelmann).

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[1] First demonstrated by Engelmann on the Bacteria.

If a capillary tube, fused at one end, be filled with a 0.05-per-cent solution of malic acid and the open end of it be placed in a drop of water containing the spermatozoids of a fern, so that the acid can diffuse gradually into the water, the spermatozoids begin at once to move toward the opening of the tube and to wander into it. The same phenomenon may be observed indeed with a much weaker solution (0.001 per cent, Pfeffer).

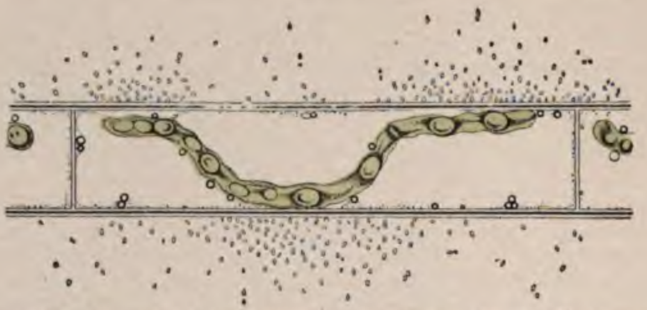

FIG. 31.—Illustrating chemotaxis. The chlorophyll bodies in the cells of *Mesocarpus scalaris* under the influence of light liberate oxygen: the bacteria are most abundant where the chlorophyll bodies lie nearest the surface—i. e., where the liberation of oxygen is most active, after Engelmann.

It has been observed that the uterus and Fallopian tubes of rabbits and rats exercise a positive chemotactic influence on the spermatozoa of the corresponding species, but that the ovary itself is entirely indifferent in this respect. Chemotaxis is of the utmost importance in the following connection also. We have seen how the leucocytes have the power to seize and consume Bacteria which find their way into the body. They are attracted to the Bacteria by substances given off by those organisms. If a capillary tube, containing a *sterilized* culture of, say *Staphylococcus pyogenes albus*, be introduced under the skin of a rabbit, after a few hours it is filled with leucocytes. The same culture fluid by itself exercises no such influence on the leucocytes.

Likewise when the leucocytes assemble in a certain place for the purpose of carrying away the products of normal or pathological tissue destruction, their migration is caused by chemotaxis (cf. page 37). In short, as far as our present information goes, we may say that *the migrations of the leucocytes are controlled, quite independently of the nervous system, essentially by chemotaxis.*

From these examples it ought to be apparent that chemotaxis plays a very great rôle in the processes of the living world, since by it the migrations of free-living cells are often controlled according to their momentary needs. It is therefore unnecessary to invoke any psychical properties in explanation of such phenomena.

In the *higher animals* the sense of smell has been developed as a special chemical sense. It is true that many of the movements taking place under its influence are to be regarded as conscious; but in many other cases they run the course of pure reflexes, and if we may extend the notion of chemotaxis to all movements which either directly or indirectly are inaugurated and controlled by chemical stimuli without the participation of consciousness, these may be regarded as to a certain extent chemotactic. Thus according to the thorough analysis of Bethe, a whole order of complicated habits of the ants might be explained as chemotactic reactions, and in the bees several habits are undoubtedly of this origin.

Jennings has shown that there is nothing specifically directive about the chemotactic effects of chemical substances on Infusoria and Bacteria. If, for example, *Bacillum volutans* be placed in a preparation with a green alga, they are uniformly distributed at first throughout the preparation. When the alga begins to give off oxygen and the bacilli come by chance into this zone rich in O_2, they swim through it to the opposite side, turn and swim again to the border, and so on incessantly, but they do not adhere to any definite orientation with respect to the middle point of the oxygen zone.

[The behavior of an Infusorian under chemical stimulation may be illustrated, according to Jennings, as follows: the usual motor response of a *Paramæcium* to any kind of an obstruction is to reverse its cilia and swim backward, then turn toward the side containing the peristome and swim forward again (Fig. 32). When in its wanderings the *Paramæcium* enters a drop of dilute acid, the chemical change of the medium does not cause the reaction, but whenever the organism attempts to leave the drop the chemical change experienced constitutes a stimulus which evokes the usual motor response, and the organism remains entrapped. Coming in contact with an alkali produces the same response and the organism turns so as to avoid the substance. The result is that the organisms collect in dilute acids, including carbon dioxide (positive chemotaxis), and refuse to do so in alkalies (negative chemotaxis). But the acid can scarcely be said to *attract* the organisms in any proper sense of the term, nor the alkali to *repel* them. They remain in the acids doubtless because these substances are favorable[1] to their life processes and avoid the alkalies because the latter are harmful.—ED.]

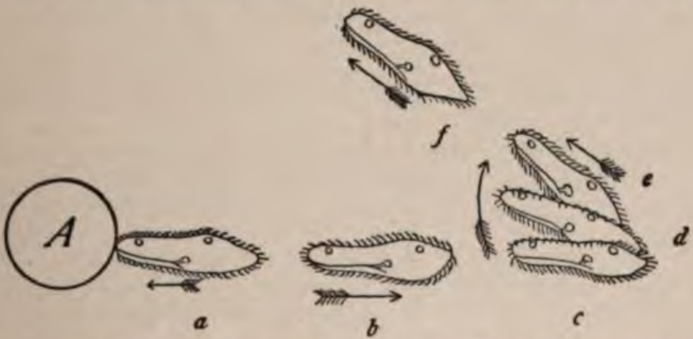

FIG. 32.—Motor response in *Paramæcium*, after Jennings. *a–f*, successive positions after meeting an obstruction, *A*.

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[1] Jennings recognizes this selection by random movements of conditions not interfering with the physiological processes as a fixed principle of behavior, not only in the Bacteria and Infusoria but in higher animals as well.—ED.

D. MECHANICAL STIMULATION

In a great many different kinds of cells the production of energy may be aroused by shocks of a purely mechanical nature. Agencies of this kind may exercise also an important influence upon the locomotion of many organisms.

In so far as they are due to gravitation these agencies are designated as *geotactic*.

The collection of Infusoria at the central end of a centrifuge (Jensen); the movement of *Paramœcium* downward in its medium in condition of hunger and of low temperature, but upward under opposite circumstances; the vertical climbing of *Cucumaria, Actinia, Asterina, Peripleneta*, etc.; the orientation of fishes; and the behavior of a decerebrated frog are instances of geotaxis. Changes of position, changes of attitude, etc., taking place among the Metazoa are to be regarded as reflexes of a complex order, analogous to those initiated by chemical stimulation (cf. page 54). It is probable that they are brought about according to the attitude of the animal by the stimulation of the end organs of different nerves (of the skin, joints, etc.) through the pressure of the body or through the pull which is exerted by unsupported parts. Finally, we should mention the otolith apparatus as a seat of peripheral stimulation (cf. Chapter XVIII).

A second form of movement produced by mechanical influence is *rheotaxis* —i. e., changes of position induced by flowing water or currents of air.

In microscopical preparations it may be shown that spermatozoa move against the current (Roth), and it has long been known that once these elementary organisms enter the oviduct they strive to reach the very end of the tube, forcing their way against the current produced by the ciliated epithelium. Wheeler has directed attention to the fact that air in motion influences the movements of insects in a similar way.

Another group of phenomena conditioned by mechanical stimulation is the following. Frog's spermatozoa when mounted on a slide bore into all the little scratches and crevices of the glass surface. These cells have therefore a decided inclination to be in contact with solid bodies (*thigmotaxis*). In line with this Jennings has found that *Paramœcium aurelia* will attach itself to solid particles in the preparation, and Pütter has demonstrated that thigmotaxis represents probably a quite general phenomenon widely distributed among all classes of the Protista.

Thigmotaxis is exhibited also by many higher animals. There are animals such as the ants, which always seek out the concave corners and edges of cavities, while other animals as constantly establish themselves on the convex edges and corners of bodies.

E. STIMULATION BY MEANS OF LIGHT

Light, if we include only the so-called illuminating rays, stimulates directly only a few kinds of cells. In higher animals it acts only upon the visual cells of the retina, on the musculature of the iris, and, if it be concentrated enough, upon the end organs of the heat nerves. Likewise the skin (of certain invertebrates at least) is sensitive to light rays. In some unicellular organisms movements have been observed which are undoubtedly induced by light. The red rays are said to exercise the most powerful influence on Amœbæ (Harrington and Leaming). In frog and triton embryos both in the egg and in the young larval stage, light calls forth pronounced movements, and in this case the blue and violet rays are most powerful (Finsen). The Rhizopod *Pelomyxa* contracts on sudden illumination. A species of *Bacterium* (*photometricum*) is stimulated to active movements by light, while in the dark it lies perfectly still. In the microspectrum (Fig. 33) the majority of these Bacteria wander into the ultra red, while another collection is formed in the orange and yellow (Engelmann).

The effects on the direction of movements produced by the light are designated by the term *phototaxis*.

Free-living unicellular organisms, inclosed in a drop of water, collect on the side of the drop turned toward the light (positive phototaxis), if the illumination is moderate. They flee from this side and collect on the opposite edge (negative phototaxis) if the illumination is strong. Thus we have in different degrees of illumination the same difference with which we have become acquainted under chemotaxis. In general the short-waved rays of the spectrum, the blue and violet, are the most important in this directive influence.[1]

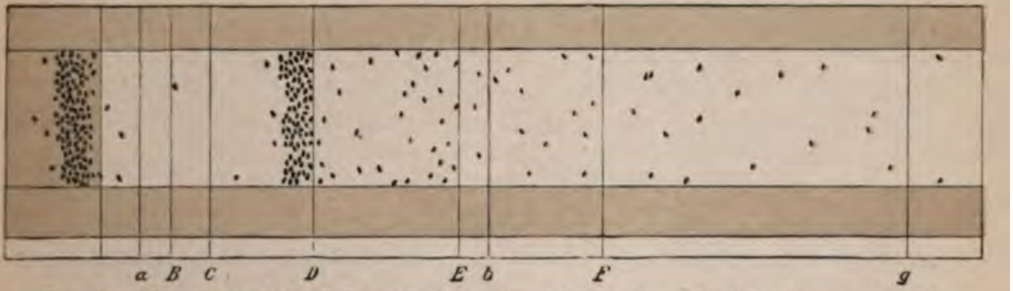

FIG. 33.—The distribution of Bacteria (*Bacterium photometricum*) in the microspectrum of direct sunlight, after Engelmann.

Loeb, Finsen, Adams, Yerkes, and others have described similar phenomena among the Metazoa. Earthworms exposed to a light varying in strength from 192 to 0.012 candle power exhibit negative phototaxis, which diminishes with the intensity of the light: in 0.011 candle power they exhibit positive phototaxis. In diffuse daylight the frog is positively phototactic: in direct sunlight it shows at first positive, then negative phototaxis.

The movements of the pigment cells of the retina by which their processes become longer and the inner ends of the cones shorter may be cited as an unmistakable example of phototaxis (cf. Chapter XXI). Even the unconscious reflex movements of the eyes, of the head and of the body as a whole, which are produced by stimulation of the visual cells of the retina by light may be regarded as in a certain measure a kind of phototaxis (cf. page 54).

The *ultra-violet rays* exercise a very marked influence on cells. On the anterior portion of the eye they produce an excitation which is characterized by catarrhal symptoms of the conjunctiva palpebralis, inflammation and swelling of the conjunctiva oculi, desquamation of the epithelium and clouding of the cornea, as well as contraction of the pupil and discoloration of the iris. Similar effects appear on the skin: it becomes red and swollen; burning sensations and sensitiveness to touch distinguish the affected portions; after some days the epidermis begins to peel off in the form of large scales, and in about fourteen days the skin becomes normal again. There usually remains for a long time, however, a light coloration of the affected part, which is sharply marked off from the surrounding skin (Widmark). With sufficient concentration of the light, the blue-violet rays also are said to exercise a similar influence (Finsen).

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[1] See note page 59.

The *X rays* discovered by Röntgen produce in the skin similar but even more powerful effects than those discussed above. Possibly the ultra-violet rays contained in the cathode rays contribute in some degree to this effect. Certain Bacteria (the cholera, anthrax, diphtheria, and tubercle bacilli) are killed by the X rays, and cells of higher plants suffer a reduction of their activities. Different Protozoa exhibit a very different power of resistance toward the X rays (of fourteen hours' duration): some forms appear not to be affected by them at all, others slightly, some very powerfully. In general it appears that forms which have vacuolated protoplasma react more quickly than those of firmer structure. The presence or absence of membranes and shells may also be significant (Schaudinn).

With respect to the *Becquerel rays* (radium) Aschkinass and Caspari have found that they weaken markedly the *Bacillus prodigiosus* in from two to four hours. With a longer exposure to radium (twenty-four and sixteen hours respectively) typhoid and cholera bacilli were killed (Pfeiffer and Friedberger). Schwarz has shown further from researches on the hen's egg that these rays destroy albuminoid bodies by a kind of dry distillation, that they decolorize luteïn and act upon the lecithin of the cell substance. In these effects he finds the explanation of the peculiar cell necrobiosis observed by Becquerel himself. Becquerel once carried in his vest pocket for only two hours a well-wrapped but highly active radium preparation. Fourteen days later he observed on the abdominal skin opposite the pocket a small burn which became larger and larger and finally developed into a deep wound which did not heal for months.

F. STIMULATION BY MEANS OF HEAT

Only in relatively few cases does heat appear to exercise a direct stimulating effect on living cells. In the higher animals only the end organs of certain afferent nerve fibers are really roused to activity by heat. Heat, as already remarked above, exercises a more powerful influence on the *excitability* of the cells. In all cells we find that the life processes increase in intensity with the temperature up to certain limits (cf. *supra* page 29), and likewise that with a lowering of the temperature they are depressed at least, if not brought to a complete standstill. It is not easy in any given case to separate clearly the actually stimulating effect from the heightening influence on the excitability, and the phenomena just mentioned are regarded by some as the expression of actual stimulation.

As an example of the directive[1] influence of heat on the movements of cells (*thermotaxis*) the behavior of the ciliate Infusorian, *Paramœcium*, may be mentioned. If the vessel in which they are contained is warmed on one side to about 24°–28° C. the animalcules withdraw to the other side, while with a temperature below this limit they wander to the warmer side—opposite movements therefore according as the same stimulus is strong or weak.

G. ELECTRICAL STIMULATION

Because they are the most easily manipulated and most easily graduated, *electrical stimuli* have been studied with very great exactness. Since their effects are investigated chiefly on nerves and muscles of the vertebrates, we shall deal with them at some length in presenting the physiology of nerves and muscles. Suffice it for the present to state that it has been found in nerves and muscles that the electrical current stimulates only at one pole or the other, at the *negative pole on closing the current*, and at the *positive on breaking it* (Pflüger). Between the two poles it acts to change the excitability, but not to stimulate.

In *Paramœcium*, excitation is said to take place with the closing of the current at the anode (Verworn). And there are other exceptions to the law as it applies to nerve and muscle. Carlgren has shown with regard to *Paramœcium*, that lifeless individuals, immediately after the closing of a sufficiently strong constant current, show at the anode a shrinking up and at the cathode bending movements, both of which are the consequence of the so-called cataphoric effect of the constant current [i. e., the tendency which this current has to sweep substances in solution along with it—Ed.]; and it is not at all improbable that similar phenomena in the living *Paramœcium* are of the same origin.

The following phenomenon might be presented as a *secondary effect* of the electric current. If a salamander (*Amblystoma*) be traversed longitudinally by an electric current, the skin glands of the animal begin to produce a copious secretion, which appears only on the side of the anode. The same occurs also with isolated pieces of the animal in which the spinal cord has been destroyed. But this secretion, as Loeb has shown, is not excited by the current itself, but by the electro-positive ions liberated by the current. For if the animal is immersed in a NaCl solution, the electro-positive ions in their migration toward the cathode are set free on the skin of the animal and are combined with the hydroxyl of water into NaOH. As direct experiments have proved, this alkali exercises a powerful stimulating effect on the skin glands;

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[1] Jennings is of the opinion that these so-called "directive influences" of light and of heat are merely other instances of the selection by random movements of conditions favorable to the life processes. Taking *Paramœcium* as an example we find that when it wanders into a degree of illumination or of temperature which is unfavorable, the organism is stimulated by the change and reacts by making the usual motor response for avoiding an obstacle. The total effect of many such responses is to carry the organism out of the field of unfavorable influences or to keep it in the field of favorable ones.—Ed.

the phenomenon is, therefore, only a secondary effect of the current. It should be remarked further that neither weak acids nor electro-negative ions exercise such an influence.

Electrical stimuli like other stimuli exercise a *directing influence on Locomotor movements.* If a constant current be passed through a vessel in which are frog tadpoles or fish embryos, the animals orient themselves with their long axes in the direction of the current, and with the head directed toward the cathode. They remain in this position as long as the current is closed; when the current is reversed the animals turn as if by command (Hermann).

Hermann explained this form of *galvanotaxis* by supposing the central nervous system to be excited by the ascending current, but to be unaffected or even paralyzed by the descending current, so that the larvæ and embryos either instinctively or reflexly take the position in which they are stimulated least. Loeb on the contrary has made it quite probable by experiments on shrimps and *Amblystoma* larvæ that the current produces parallel changes of tension and energy production in associated groups of muscles, the result of which is that the movement toward one pole is facilitated, but movement toward the opposite pole is impeded. Thus with the shrimps the tension of the flexors predominates on the side of the anode, while the tension of the extensors predominates on the side of the cathode. With a current of medium strength the animals always move toward the anode; if when the current is turned on the head end is already near the anode, the change in position is effected by a forward movement; if the tail end lies nearer the anode, it is effected by a backward movement.

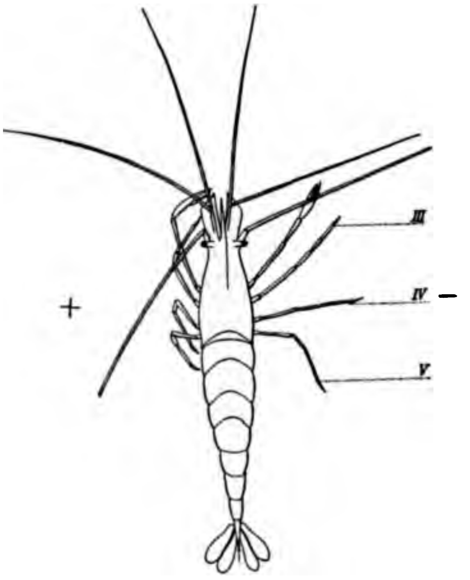

Fig. 34.—Showing the effects of a constant current on the shrimp *Palæmonetes*, when the current passes transversely through the animal's body, after Loeb and Maxwell. The legs on the side of the anode are strongly flexed, those on the side of the cathode are strongly extended.

The following examples of galvanotaxis may be mentioned. Certain echinoderms in their youngest and oldest stages (free-swimming gastrulæ and the creeping mature animals) exhibit no galvanotaxis, while in the intermediate stages (free-swimming plutei and bipennaria) they exhibit very marked galvanotaxis, and wander to the cathode (Carlgren). The majority of ciliate Infusoria and Amœbæ assemble at the cathode, if an electric current is conducted through the vessel in which they are contained. Many flagellate Infusoria show the opposite reaction by moving to the anode. Finally, it has been observed that the ciliate Infusorian *Spirostomum* places itself with its long axis at right angles to the current (Verworn). All these differences find an explanation according to Wallengren in the general fact that in all ciliate Infusoria the cilia on the side of the cathode beat toward the anterior end, those on the side of the anode, toward the posterior. For example, as long as its anterior end is directed toward the cathode, *Opalina ranarum* (Fig. 35) always turns toward the right as indicated by the arrow.

Organisms are killed by strong electric currents. Concerning the changes effected by such currents on the higher animals, Prevost and Battelli especially have made extensive investigations, of which the following, relating to the dog only, will be mentioned here. With an induction current of lower tension (up to 120 volts) death results from *fibrillary contractions of the heart* produced by the current, in consequence of which the circulation is ultimately stopped (cf. Chapter VI). The disturbances in the nervous system coming on at the same time, indicated by convulsions and the like, have relatively little importance. Respiration is resumed after a temporary pause, and may even continue for two or three minutes after the inception of fibrillary contractions of the heart.

With induction currents of higher tension (more than 1,200 volts) death occurs as a result of *paralysis of respiration*, while the ventricles beat rapidly and powerfully and the auricles stop in diastole. Indeed by means of currents of high tension one may even restore a heart seized with fibrillary contractions to its former functional power, when it cannot be restored to its normal action in any other way.

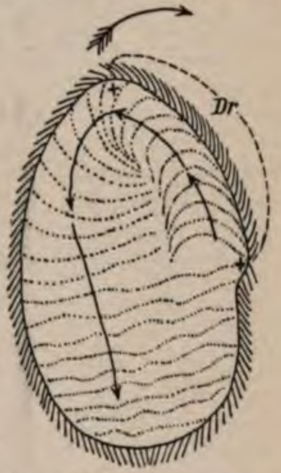

FIG. 35.—*Opalina ranarum*, a ciliated organism from the intestine of the frog, seen from above, after Wallengren. *Dr*, the cilia used by the organism in changing direction to the right.

Strong induction shocks (Rhumkorff, 45 cm. spark, twenty interruptions per second, primary current twenty-five volts) can be conducted from mouth to rectum for one and one-half minutes without danger to the animal. In two and one-half minutes he dies in convulsions produced by failure of respiration; if artificial respiration is maintained the animal can survive such currents acting for ten minutes.

The effect of the electric current is dependent not only upon its tension, but also upon its duration and the place of its application, as well as upon contact between the electrodes and the body. The different animal species also exhibit differences in sensitivity: the dog appears to be the most sensitive, the horse less so, still less the guinea pig, rabbit and mouse.

H. COSMIC INFLUENCES

It has long been firmly established by general experience that cosmic forces exercise a marked influence upon organisms; and to convince ourselves of such influence we have only to be reminded of the pains affecting gouty and rheumatic individuals with different conditions of weather. We know very little at this time about the real nature of these agents. Recently Arrhenius has sought to bring various physiological processes, notably menstruation, into relation with electrical variations of the atmosphere and the chemical changes thereby effected. But the results thus far obtained on this subject appear to be too limited to justify a fuller presentation in this book.

I. CONDUCTIVITY

Besides these artificial stimuli which are able to excite the cells or to increase their excitability, there occurs in the Metazoa a form of stimulus which belongs to the body itself, namely, the *stimulation of one cell by another*. It is in this connection that the nerves are of the very greatest importance; they transfer their excitations to the end organs, the muscle cells, gland cells, etc.; or they are themselves stimulated by other cells, as when the sensory nerve fibers are roused to activity by their peripheral end organs, or when a nerve cell by means of its processes arouses another cell to a state of activity. Here belongs also the case of the stimulation of a smooth muscle cell by its neighbor, which in all probability is accomplished by means of the protoplasmic connections (intercellular bridges) which have been demonstrated between these as well as between other kinds of cells (cf. Fig. 36). This form of stimulation represents one of the most important mechanisms by which the different parts of the Metazoan body are made to coöperate harmoniously.

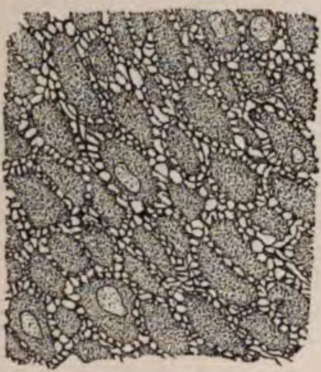

FIG. 36.—Cross section of the intestinal musculature of the cat, after Boheman. The dotted areas represent cross sections of muscle-cells, the black lines between them represent intercellular bridges.

The stimulus is transmitted from one part to the other also in a single cell. The clearest example of this we have again in the nerves, which are nothing else than long processes of nerve cells, and they propagate a stimulus directly transmitted to them by passing it along from one section to the next throughout its entire length. We meet with the same mode of transmission wherever a cell is stimulated at one definite point and the excitation extends throughout the entire cell body.

J. THE ASSIMILATIVE PROCESSES INDUCED BY STIMULATION

Our knowledge of the *assimilative processes* induced by different stimuli is still very imperfect.

With respect to the question of most interest to us, namely, the influence of stimuli upon the formation of living substance, we know that the Bacteria and Infusoria multiply rapidly as the result of increasing the supply of nourishment, and that the sunlight gives the impetus for the formation of the green coloring matter of plants; for germinating seeds develop in the dark into a white or whitish seedling which becomes green only when it is exposed to the light. Since the chlorophyll bodies are to be regarded as composed of living substance, we have in the latter instance a case where an external stimulus actually effects the formation of living substance. As regards the first example, one might say that the abundant supply of nourishment had given the impetus for a more active formation of living substance; but the matter is not entirely clear, for it might also be that the impulse to multiply in these organisms is just as great with scanty as with abundant nourishment, only with a deficiency of nutrient substances it cannot be manifested.

From observations on the storage of substance in the bodies of young animals it appears that the *inherent growth energy* is of much greater importance than any form of external stimulation. But in mature animals, if any increase in the living substance takes place under normal circumstances, we think of it at once as being caused by some agency outside the cells themselves; and hence its consideration properly belongs under the present topic. Now results of metabolism experiments show that ordinarily the cells (of the higher animals at least) destroy practically all of their daily supply of proteid nourishment, but that under certain circumstances (not too great age, and great excess of potential energy in the food, cf. page 120) they store some of the proteid. It appears in fact that in spite of their inner propensity to destroy proteid, an abundant supply of nourishment in some way makes it possible for the cells to change dead proteid into living protoplasm. If this is correct—and the question can scarcely be regarded as finally settled—this storage would be the consequence of a chemical stimulation brought about by the excess of proteid.

However this may be, the only really effective way known to us of increasing the living substance in the mature higher animals is *work*; and it is possible to conceive of this also as a special form of chemical stimulation. A grown man may eat ever so much food, his diet may be adapted perfectly to the purpose, but no significant increase of muscle substance will take place if the muscle does not accomplish sufficient work; whereas a working muscle increases both in power and in volume—i. e., the work has called forth an increase of living substance. Since now every muscular movement is originated by the motor nerves, and since experience shows that a nonworking muscle always decreases in volume, and a muscle paralyzed by cutting its motor nerves undergoes atrophy and degeneration in a relatively short time, it follows that *some kind of a nutrient or trophic influence on the muscle must be exercised by the central nervous system through the motor nerves.* What the nature of this influence is, we cannot say definitely. Since, however, the stimuli originating in the body itself are in general of a chemical nature, we may perhaps conclude that the trophic influence mediated by the nerves is a chemical stimulus. Other facts which we shall discuss somewhat in detail in what follows show that an influence of a similar nature is exerted on other organs by the nerves belonging to them. If the cerebral secretory nerve of the submaxillary gland be cut, the gland atrophies. This nerve is therefore of great importance for the maintenance of this part of the body, although it does not follow with certainty from the foregoing that it has contributed also to the formation of living substance.[1]

With regard to the *original formation of cells and tissues*, there are numerous data which go to show that the most widely different stimuli can effect an essential modification of the growth process.

Here belong the effects of gravitation (*geotropism*), and other mechanical agencies (*rheotropism, thigmotropism*), of light (*heliotropism*), and of galvanism (*galvanotropism*) upon the orientation of plants and of various sessile animals.[2]

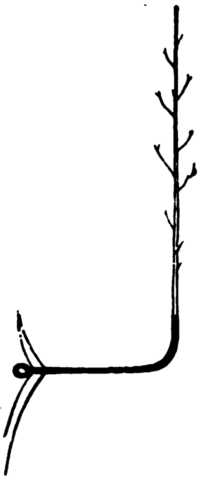

FIG. 37.—A shoot of *Antennularia antennina*, a small hydroid animal, exhibiting negative geotropism, after Loeb.

The following may be mentioned as examples. The stems of plants grow away from the center of the earth (negative geotropism), the roots toward the center of the earth (positive geotropism). If germinating seeds be placed on a wheel rotating rapidly in a vertical plane so that the influence of gravitation is overcome, the stem grows toward the middle point of the wheel, the roots turn away from it i. e., the stem grows in the direction of least pressure, the root in the direction of the greatest (Knight).

The hydroid polyp (*Antennularia antennina*) consists of a central stem of 1–2 mm. thickness, and often more than 20 cm. in length, which generally grows perfectly straight up from a tangle of very thin filamentous rootlets. If now an *Antennularia* whose stem is in process of growth be brought into a position deviating from the vertical, the growing tip bends until it finds the vertical direction again, and then grows directly upward. The root on the other hand grows vertically downward but not in so straight a line as the stem (cf. Fig. 37).

Rheotropism.—Seedlings of maize and other plants germinated in a tub of flowing water grow with roots parallel to the surface of the water and against the current. The hydroid polyp, *Eudendrium*, also bends in its growth against the current (Loeb).

Thigmotropism.—Numerous plants twine around the vertical stems of other plants and so climb upward.

Heliotropism.—The growing parts of a plant always turn toward the light.

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[1] Perhaps a clearer case of the influence of nervous tissue on the formation of living substance is that of the regeneration of a " head " in a simple worm. C. M. Child has shown that if the anterior end of the flatworm *Leptoplana* be cut off in such a way as to leave the collection of ganglion cells which serves the animal as a " brain," the animal will regenerate a new " head "; but if the cephalic ganglia be removed with the anterior end no " head " is regenerated, because in this instance the anterior end is no longer capable of functioning as a " head." In other words, the determining factor in the formation of the living substance here, as in the mammalian muscle, is the motor activity dependent upon the nervous system, or, as we have just learned, a special kind of chemical stimulus.—ED.

[2] With Herbst I employ the term geotaxis, galvanotaxis, etc., for the effects on the movements of free-living organisms brought about by external stimuli, and the terms geotropism, galvanotropism, etc., for the changes in growth brought about by external stimuli. The former phenomena are purely dissimilative, the latter are essentially assimilative. These phenomena could only be produced by the constant effect of these stimulating agents acting in a perfectly definite manner.

Indeed, in many plants one may observe that on a sunny day the whole course of the sun is followed by appropriate movements of the plant. This effect is brought about chiefly by the more strongly refractive rays of the spectrum.

Galvanotropism.—With long exposure to a constant current root tips turn toward the cathode.

Even in the highest animals we meet with extensive regenerative processes which, in part at least, are caused by a kind of chemical stimulation. Thus if a large part of the liver be cut away, a considerable regeneration of liver tissue follows (Ponfick, Podwyssozki). After extirpation of one kidney, the remaining kidney increases considerably in volume by new formation of kidney tissue. Numerous discoveries of the pathologists on abnormal growths belong here also.

Among the Mammalia, however, the powers of regeneration are relatively small in comparison with those of the lower vertebrates and especially of certain invertebrates and of plants, for in the former the tendency to regeneration is limited to certain tissues, while in the latter whole organs may be formed anew.

The tendency to the *syntheses of nonliving substances* in the organism appears to be favored to a certain extent by a rich supply of food. In an atmosphere rich in CO_2, under otherwise similar conditions, plants show a greater production of starch; and with an abundant supply of carbohydrates animal cells form fat which is stored up in the fat cells. Animal cells carry on also a multitude of other syntheses the stimulus to which might well be sought for in a chemical excitation effected by the substances supplied them. Anything more exact than this is quite beyond our knowledge at this time.

K. PARALYSIS AND FATIGUE

We meet with a true case of *paralysis* when a dissimilative stimulus is carried beyond a certain strength. This is true of all kinds of stimuli and for all kinds of cells, in so far as they can be roused to a state of activity by the particular stimulus. If the strength of the stimulus be not too great, nor its duration too long, complete restoration may take place after its cessation. But if the stimulus be too strong or if it last too long, it has a fatal effect on the protoplasm.

Certain chemical substances—e. g., the *narcotics*, to which belong alcohol, ether, chloroform, morphine, cocaine, paraldehyde etc.—are characterized by their paralyzing effects, obtained even with small doses. After a short period of excitation, the protoplasm exposed to these substances loses to a greater or less extent its vital activity. With small doses and short exposure the paralysis passes off, but with large doses or long exposure the paralysis becomes more and more profound until death finally ensues.

Fatigue may be considered as a special kind of paralysis. In all living beings (though in different genera and individuals in different degree) there always occurs after a sufficiently intense dissimilative activity *a reduction of the functional power*, as a consequence of which the same strength of stimulus produces a much weaker effect than before. If the stimulation be continued long enough, the excitability may be entirely destroyed. All these phenomena which are best known in man from his subjective experience of the results of severe muscular work are included under the term *fatigue*.

Now it has been shown that fatigue, for the most part at least, *is caused by the products formed in metabolism* (J. Ranke), as may be seen from such facts as the following: if the blood of an exhausted dog be injected into a vein of a fresh dog, the latter immediately exhibits very evident signs of fatigue.

If a fatigued organ be allowed to rest for a long time a remarkable thing occurs: the organ completely recovers—i. e., its former *functional power has returned*. This is not difficult to explain for the free-living unicellular organisms; for they give off the decomposition products to the surrounding medium in a very simple manner. And even in the higher animals the recovery after fatigue presents no great difficulties, for the waste products are carried away from the organ by the circulation of the blood and lymph, and at the same time the blood places new nutrient material at its disposal. The same phenomenon is observed however in the organs of cold-blooded animals which have been cut out of the body. A frog's muscle which by repeated stimulation has been brought to a condition where it cannot contract at all, recovers and becomes functional again in spite of the fact that there is no circulation to carry away waste products. It follows therefore that recovery is not conditioned solely upon the removal of waste products, but that other factors also must be taken into account, with which we are not yet thoroughly acquainted.

§ 4. DEATH

We have seen that the most widely different external agencies of sufficient intensity and sufficient duration have the power to check life and to bring on death. Changes also which are going on in the cells without any such external influences can reduce their functional powers. In the course of life these alterations come on gradually, in some beings more rapidly than others, but always inevitably. They are known by the term *senescence*. If they progress far enough, death ensues as the result of old age. This form of death is, in man at least, only rarely to be considered; for the body is subjected to many external accidents of all kinds, and only in the most exceptional cases does it escape all of them. The senescent changes, however, play an important rôle even here, for by their influence the power of resistance of the organism to the accidents which it must encounter is more and more reduced.

After death the body is destroyed as a rule within a short time, partly by autolysis of the organs (cf. page 38), partly by processes of decomposition and putrefaction which are carried on by the lowest organisms. The carbon and hydrogen of the body pass off in the atmosphere as carbon dioxide and water vapor; and the nitrogen and sulphur, after a series of transformations taking place under the influence of Bacteria, are combined with metals in the form of nitrates and sulphates which are taken up by the water of the soil. These substances, carbon dioxide, water, nitrates and sulphates are the normal food of green plants, and by the synthetic processes going on within them are combined again into starch, fat and proteid. Thus they are in condition once more to serve as food for animals and thus the organic elements complete a circulation between animals and plants, which is interrupted by the circumstance that the synthesis going on in plants can take place only under the influence of sunlight. The entire living world represents, therefore, a collective whole in which every living being fulfills its special purpose as a link in the chain.

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CHAPTER III

THE CHEMICAL CONSTITUENTS OF THE BODY

As already observed at page 20 we know nothing at all concerning the chemical nature of the living protoplasm. And yet from the dead body we are able to isolate a number of substances derived from the living protoplasm. The most important of these are the simple and the compound proteids. Many substances occur also as nonliving cell contents and as specialized products or as assimilative products, part of which are closely related to the proteids, while part have an entirely different constitution. Here belong the gelatin-forming substances, fats, carbohydrates, the enzymes, the products of internal secretions (cf. Chapter XI), etc. Finally there are found in the body itself as well as in its secretions and its excretions, numerous substances which owe their origin to the dissimilative processes of the body. These latter substances, as well as the enzymes and the products of the internal secretions, will be discussed later in connection with the physiological processes involved, but it will be appropriate to treat here the products of the assimilative activity of the cells, and the final decomposition products of protoplasm so far as they are yet known to us.

§ 1. THE NITROGENOUS SUBSTANCES

A. THE SIMPLE PROTEIDS

In the purest state obtainable proteids are colloidal, slightly or not at all diffusible, lævo-rotatory bodies of high molecular weight, without smell, without taste, and as a rule amorphous. In the dry condition they are either white or yellowish powders, or are made up of solid yellowish disks transparent in thin layers. Crystallized proteid has been obtained from plant seeds and from egg albumin (Hofmeister), from whey (Wichmann), and from serum albumin (Grüber) (Fig. 38).

Proteids exhibit great differences with respect to their solubility: some are soluble in water, others in solutions of neutral salts, others again in weak alkaline or weak acid solutions, and some are not soluble in any of these fluids.

The last mentioned can be dissolved, in part at least, by means of strong acids or bases, but they at the same time undergo a transformation, and instead of the original proteid substances we then have what are known as *modified proteids.*

Proteids which are dissolved by means of the above-named indifferent solvents can be isolated from the tissues and fluids of the body probably unchanged, and are therefore designated as *native proteids.*

The *solubility* of these substances is intimately related to their acidic or basic character. Proteids react with both acids and bases forming salts, and themselves therefore partake of the nature of both bases and acids. The acidic and basic characters, however, are not equally developed in all proteids. Those in which the two are approximately equal have a neutral reaction and are soluble in water and in solutions of neutral salts. Others react as weak acids, are insoluble in neutral fluids, but are soluble in weak alkaline solutions, and are precipitated from the latter by weak acids. Others again react as weak bases, are soluble in weak acids and are precipitated by weak bases.

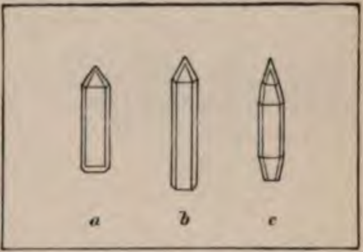


FIG. 38.—Crystals of serum-albumin, after Wichmann.

The proteids are *precipitated* from their solutions by various reagents, the reactions being for the most part traceable to their double character as acids and bases. As acids they form with the salts of the heavy metals precipitates of insoluble proteid-metal salts. As bases they form insoluble salts with numerous weak acids, such as tannic acid, phospho-tungstic acid, hydroferrocyanic acid (the so-called alkaloid reagents). Proteids cannot be recovered unchanged from these precipitates; they have been modified by the reactions.

Proteids are precipitated and at the same time modified by strong mineral acids (e. g., Heller's test with HNO_3) and by alcohol. They are modified also by heating their solutions. If a proteid in solution is treated with a concentrated solution of certain neutral salts of the alkalies or metallic earths —particularly ammonium, magnesium or sodium sulphate—or with these salts in substance, it separates out unmodified—i. e., is "salted out." The concentration of the neutral salt necessary for salting out varies greatly for different proteids, and we have in this circumstance a method of separating different proteids in the same solution from one another.

The chemical elements characteristic of simple proteids are C, N, S, H and O. A compound in which no S is found ought not to be described as a true proteid.

The percentage composition of the proteids, which consist of these five elements only, varies within rather narrow limits:

C	50.6–55.0	per cent	....	average,	52	per cent.
H	6.5– 7.7	"	....	"	7	"
N	15.0–18.5	"	....	"	16	"
S	0.3– 2.2	"	....	"	2	"
O	20.5–23.5	"	....	"	23	"

On burning proteid, various mineral constituents remain as the ash. These it appears cannot be completely removed from proteid without changing its composition. Yet in none of the analyses of proteid has the ash been taken into account.

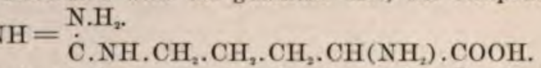
Investigators have subjected proteids to various treatments, particularly hydrolytic cleavage, and have sought to determine the resulting cleavage products both qualitatively and quantitatively, hoping thus to arrive at the constitution of the proteid molecule. In this way it has been shown that certain groups of atoms are present in all proteid substances, while others occur only in some and are therefore not characteristic of the proteids as a group. Such compounds as contain the smallest number of atomic groups and at the same time give all of the general proteid reactions would be classed by this method as simple proteids. The compound proteids would be formed by addition of new groups of atoms to the simple proteid molecule.

The atomic groups thus far known as characterizing the proteids are the following (Hofmeister).

1. The guanidin rest—$\mathrm{CNH.NH_2}$.

2. Monobasic α-monamino acids of the series $C_nH_{2n+1}NO_2$, such as amino-acetic acid (glycocoll, $\mathrm{CH_2(NH_2).COOH}$), amino-propionic acid (alanin, $\mathrm{CH_3.CH(NH_2).COOH}$), amino-butyric acid ($\mathrm{CH_3.CH_2.CH(NH_2).COOH}$), amino-valerianic acid ($\mathrm{CH_3.CH_2.CH_2.CH(NH_2).COOH}$), amino-caproic acid, isobutyl-amino-acetic acid (leucin, $\mathrm{(CH_3)_2.CH.CH_2.CH(NH_2).COOH}$). Of these compounds leucin, glycocoll and alanin occur most abundantly, amino-valerianic acid and amino-butyric acid less frequently. Certain of them are wanting in various proteids.

3. Monobasic α-ω-diamino acids of the series $C_nH_{2n+2}N_2O_2$: e.g., the α-δ-diamino-valerianic acid ($\mathrm{CH_2(NH_2).CH_2.CH_2.CH(NH_2).COOH}$) and the α-ϵ-diamino-caproic acid (lysin, $\mathrm{CH_2(NH_2).CH_2.CH_2.CH_2.CH(NH_2).COOH}$). The former is always associated with the guanidin rest, the compound being described as *arginin*:



$$\mathrm{NH}=\overset{\mathrm{N.H_2.}}{\dot{\mathrm{C}}}\mathrm{.NH.CH_2.CH_2.CH_2.CH(NH_2).COOH.}$$

Arginin and lysin occur in varying proportions in all proteids (Drechsel, Hedin, Kossel), although as an exception one of them may be entirely absent, as lysin from zeïn. They are particularly abundant in the *protamins*, first obtained by Miescher from fish sperm, and described by Kossel as the simplest proteid. This designation, however, is not admissible since protamins do not contain sulphur.

4. A monobasic β-oxy-α-monamino acid, namely, the β-oxy-α-amino-propionic acid (serin, $\mathrm{CH_2(OH).CH(NH_2).COOH}$), has been demonstrated so far in serum albumin, globin and edestin, and probably occurs in the other simple proteids, since it was found in casein and in fibroïn of silk (Fischer).

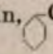
5. A monobasic β-thio-α-monamino acid: namely, the β-thio-α-monamino-propionic acid ($\mathrm{CH_2(SH).CH(NH_2).COOH}$), corresponding to serin, which probably enters into proteids as the disulphide (cystin, $\mathrm{COOH.CH(NH_2).CH_2{-}S{-}S{-}CH_2.CH(NH_2).COOH}$) (K. A. H. Mörner, Embden). Mörner finds that the total sulphur of keratin (cow's horn, human hair), serum albumin, and serum globulin might occur as cystin groups. In the shell membrane of the hen's egg as much as three-fourths of the sulphur are present as cystin, in fibrinogen about one-half, and in egg albumin only about one-third. How the remaining sulphur is combined in these and other proteids, we do not know.

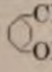
6. Dibasic α-monamino acids of the series $C_nH_{2n+1}NO_4$. namely, amino-succinic acid (aspartic acid, $\mathrm{COOH.CH_2.CH(NH_2).COOH}$) and amino-pyrotartaric acid (glutamic acid, $\mathrm{COOH.CH_2.CH_2.CH(NH_2).COOH}$). The per-

centage of monamino acids in the proteid molecule is by no means small: 60.2 per cent of the total nitrogen in crystallized serum albumin, 67.8 per cent in crystallized egg albumin, 55.0 per cent in crystallized edestin, 68.3 per cent in serum globulin (horse).

7. Carbohydrate groups. In many proteids, but not in all, there is a nucleus which on total cleavage appears regularly as glucosamin ($CH_2(OH).CH(OH).CH(OH).CH(OH).CH(NH_2).CH{:}O$) (F. Müller). Besides this nucleus, or in its place, nitrogenous or nonnitrogenous carbohydrate complexes may also be present.

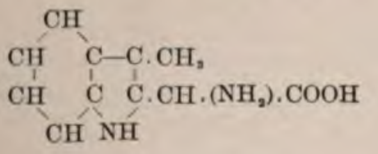
Among the simple native proteids there appears to be only one thus far known, namely, edestin, which contains no carbohydrate group in its molecule. In the others the number of these groups varies considerably. Crystallized egg albumin contains at least 10.0 to 11.0 per cent of glucosamin, submaxillary mucin 20.8 per cent of reducing substance, pseudomucin from ovarial cysts 30.0 per cent, egg mucoid 34.9 per cent, and the mucin of sputum 36.9 per cent. In crystallized serum albumin the content is very small.

8. A monamino acid of the benzol series, namely, the para-phenyl-amino-propionic acid (phenylalanin, $CH_2.CH(NH_2).COOH$) and

9. The corresponding para-oxy-compound, ρ-oxy-phenyl-amino-propionic acid (tyrosin, $CH_2.CH(NH_2).COOH$)
OH.

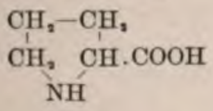
In most proteids tyrosin occurs in far greater quantity than phenylalanin. The maximal yield of tyrosin is 1.5 per cent in crystallized egg albumin, 2.0 per cent in serum albumin, 3.0 per cent in fibrin, 6.3 per cent in thymus histon and 10.1 per cent in zeïn.

10. From numerous observations on the cleavage products formed in putrefaction of proteid, it appears that an indol nucleus is present. It is likely that this nucleus in very small quantities is changed into β-methyl-indol-amino-acetic acid (tryptophan,



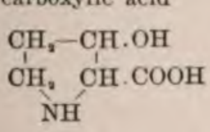
Hopkins and Cole).

11. The heterocyclic pyrrolidin nucleus is represented among the cleavage products of different proteids (edestin, serum albumin, serum globulin, egg albumin, fibrin) by the α-pyrrolidin-carboxylic acid



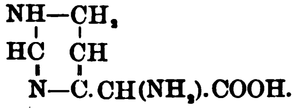
and

12. By the oxy-α-pyrrolidin-carboxylic acid



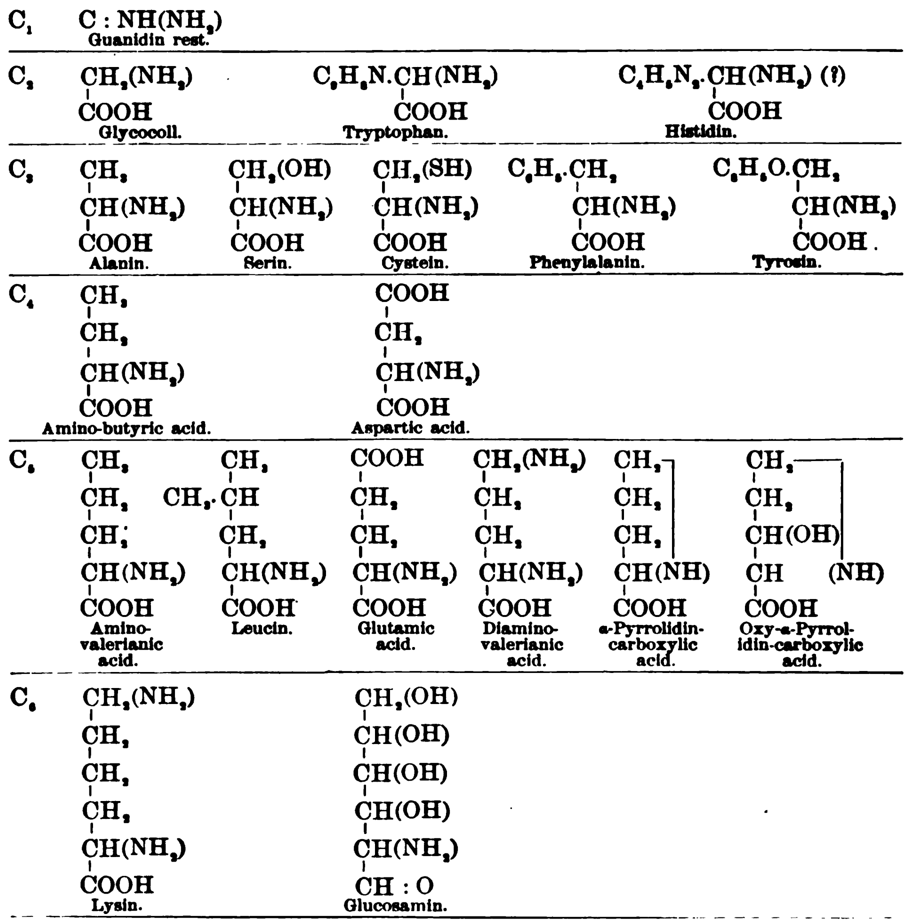
(Fischer).

13. In many proteids the presence of a hexone base, described as ***histidin***, $C_6H_9N_3O_2$ has been demonstrated. It appears to be a pyrimidin derivative



$$\begin{array}{l} NH-CH_2 \\ \;\,| \qquad | \\ HC \quad CH \\ \;\,\| \qquad \| \\ N-C.CH(NH_2).COOH. \end{array}$$

In the following table are brought together after Ehrström the most important nuclei occurring in the proteid molecule, arranged according to the number of carbon atoms which they contain.



C_1 $C:NH(NH_2)$ Guanidin rest.

C_2 $CH_2(NH_2)-COOH$ Glycocoll. $C_8H_6N.CH(NH_2)-COOH$ Tryptophan. $C_4H_5N_2.CH(NH_2)\ (?)-COOH$ Histidin.

C_3 $CH_3-CH(NH_2)-COOH$ Alanin. $CH_2(OH)-CH(NH_2)-COOH$ Serin. $CH_2(SH)-CH(NH_2)-COOH$ Cystein. $C_6H_5.CH_2-CH(NH_2)-COOH$ Phenylalanin. $C_6H_5O.CH_2-CH(NH_2)-COOH.$ Tyrosin.

C_4 $CH_3-CH_2-CH(NH_2)-COOH$ Amino-butyric acid. $COOH-CH_2-CH(NH_2)-COOH$ Aspartic acid.

C_5 $CH_3-CH_2-CH_2-CH(NH_2)-COOH$ Amino-valerianic acid. $CH_3-CH_3.CH-CH_2-CH(NH_2)-COOH$ Leucin. $COOH-CH_2-CH_2-CH(NH_2)-COOH$ Glutamic acid. $CH_2(NH_2)-CH_2-CH_2-CH(NH_2)-COOH$ Diamino-valerianic acid. $CH_2-CH_2-CH_2-CH(NH)-COOH$ α-Pyrrolidin-carboxylic acid. $CH_2-CH_2-CH(OH)-CH\ (NH)-COOH$ Oxy-α-Pyrrolidin-carboxylic acid.

C_6 $CH_2(NH_2)-CH_2-CH_2-CH_2-CH(NH_2)-COOH$ Lysin. $CH_2(OH)-CH(OH)-CH(OH)-CH(OH)-CH(NH_2)-CH:O$ Glucosamin.

Certain of these groups can be recognized by characteristic color reactions. (1) The *xanthroproteïc reaction* gives a yellow color with strong nitric acid; after neutralization with ammonia or a caustic alkali, the color passes over to orange or reddish brown. The reaction depends upon the presence of the benzol ring in the proteid molecule (phenylalanin, tyrosin, indol). (2) *Millon's reaction* gives a red coloration to the precipitate or to the fluid, when a solution of mercuric nitrate containing some nitrous acid is added to a solid proteid or to a proteid solution. This indicates the presence of the oxyphenyl group (tyrosin). (3) The *reaction of Adamkiewicz* gives a reddish violet color with 1 vol. concentrated H_2SO_4 and 9 vol. acetic acid containing some glyoxylic acid, and characterizes the indol group (tryptophan). (4) By means of *Molisch's reaction*, which is a violet color with concentrated H_2SO_4 and α-naphthol, the carbohydrate groups are demonstrated, and (5) *by boiling with alkali and a lead salt* (formation of black lead sulphide) the cystin groups are detected.

The *biuret reaction* gives a color changing from red through reddish violet to violet blue, on addition of dilute solution of copper sulphate to a proteid solution previously alkalized with caustic potash or soda and then warmed. It is very generally regarded as specifically characteristic for the proteids. This reaction, according to H. Schiff, appears with those substances which contain two $CO.NH_2$, $CS.NH_2$-, $C(NH).NH_2$-, or, under certain conditions, -$CH_2.NH_2$- groups, joined together by their own C atoms, or by a C atom in a CH-, CH(OH)-, CO group, or finally by a N atom in an NH group. However, this reaction is not a positive criterion of the proteid nature of a body, for on the one hand substances of so simple a structure as the glycinamid give it, and on the other, it is wanting with the desamido-albumin (obtained by the action of nitrous acid) where all the carbon nuclei of the proteid are present.

As a matter of fact there is at this time no physical or chemical feature by which one can decide positively whether a compound is to be described as a proteid or not; and for this reason certain substances are by some enumerated among the proteids, while by others their proteid nature is positively denied.

After discussing exhaustively all the facts obtained from the cleavage products of proteids, Hofmeister reaches the conclusion that proteids arise chiefly by condensation of the α-amino acids, union taking place regularly and repeatedly by means of the CO-NH-CH = groups. He remarks, however, that this conception of the subject does not explain all forms of linkage in proteid and that, considering our incomplete knowledge of the proteid molecule, other relations are by no means excluded.

A rational classification of the simple proteids can only be carried out when we possess more exact knowledge of their constitution, and are thus able to state what nuclei occur in each individual proteid and in what quantity. This is far from possible as yet, and with most proteids we are not even in position to say whether they are actually chemical individuals or are mixtures of different substances. We are compelled therefore to classify the proteids according to their relative solubility and precipitative reactions. This is by no means a scientific principle of classification, but it is justifiable on purely practical grounds.

Accordingly simple proteids have been divided into the following groups:

A. *Native proteids.* These are obtained from the tissues and fluids of the body by neutral chemical reagents: the albumins, globulins and mucins are the most important.

1. *Albumins:* soluble in water; not precipitated from aqueous solutions by small quantities of acids or alkalies, but precipitated by larger quantities of certain acids and metallic salts. On boiling, the solutions are coagulated if salts are present. They are precipitated by NaCl or by $MgSO_4$ only on addition of acetic acid. They are not salted out by half-saturation of their solutions with ammonium sulphate, but are so separated with greater concentration of the salt.

Albumins occur chiefly in the animal fluids. To this group belong serum albumin, egg albumin, albumin of milk, etc.

2. *Globulins:* insoluble in water; soluble in dilute salt solutions, from which they are precipitated by further dilution. Solutions are coagulated by boiling. Soluble in water on addition of very small quantities of acid or alkali, whence they are precipitated by neutralization. Likewise when solution is effected by minimal quantities of alkali, they are precipitated by carbon dioxide and are redissolved by excess of the same. Complete precipitation by saturation with $MgSO_4$, partial, by saturation with NaCl. They are salted out by half-saturation with ammonium sulphate.

This characterization of the globulins however is no longer sufficient, for it appears from several recent researches that among the compounds which are precipitated by fractional salting out of the globulins in the blood, there occur substances which are neither insoluble in water nor precipitated from their solutions with carbon dioxide. The only positive distinction between albumins and globulins therefore consists in their relation to neutralization, and especially to ammonium sulphate: the globulins are precipitated by half-saturation, the albumins are not.

The globulins also occur chiefly in the fluids of the animal body; but they may be obtained from the tissues. To this group belong fibrinogen and serum globulin of the blood, myosin and myogen of the muscles, etc.

3. *The true mucins* are substances insoluble in water and in solutions of neutral salts, but soluble with very little alkali. The solutions are viscous, and form with acetic acid a precipitate not soluble in an excess of the acid. Chemically the mucins are characterized by their high content of the carbohydrate groups. The true mucins occur in the submaxillary saliva, in the umbilical cord (Wharton's jelly), etc.

The so-called *mucoids* are distinguished from the true mucins in certain respects which are not yet definitely understood. They are obtained from the ovarial fluids, from the cornea, the vitreous body, the urine, etc.

It is also asserted that the mucins contain fat. If the submaxillary mucin be first extracted with ether and be then digested with pepsin-HCl, one can later extract with ether more than three per cent fat from the substance (Nerking).

B. *Simple proteids which can be split off from compound proteids.* Here belong globin from hæmoglobin, the proteids from the mucins, etc.

C. The native proteids are changed by the action of alkalies and acids in sufficient concentration into *alkali* and *acid albuminates* (syntonin). In the formation of alkali albuminates some nitrogen is split off from the proteid, and with stronger action of the alkali some sulphur also is separated.

In spite of their different modes of formation, and in spite of different chemical constitutions, the alkali and acid albuminates are very closely related to each other. In water or dilute NaCl solution they are almost insoluble, but are soluble on addition of small quantities of acid or alkali. Such a solution (even if neutral) is not coagulated on boiling, without the addition of sufficient quantity of neutral salts. Solutions of albuminates are precipitated at room temperature by neutralization, by excess of mineral acids, by many metallic salts. An acid solution of albuminate is readily precipitated by NaCl, an alkaline solution only with difficulty.

D. Under the influence of the digestive fluids there are formed by hydrolytic cleavage of the proteids a number of new substances, the so-called *albu-*

moses and *peptones* which will be fully treated in our study of digestion (Chapter VII).

E. Finally, we should mention the compounds arising *by coagulation of the soluble proteids,* whose properties are less well known than those of other proteid substances. To this group belongs also the *fibrin* formed in the coagulation of the blood by splitting of fibrinogen (see Chapter V).

In order to give a more exact idea of the quantitative composition of the simple proteids, we have brought together in the following table the results of analyses by Aberhalden.

PERCENTAGE OF	In Casein.	In Gelatin.	In Elastin.	In Globin from Hæmaglobin.	In Edestin.
Glycocoll	0	16.5	25.75	0	3.8
Alanin	0.9	0.8	0.58	4.19	3.6
Leucin	10.5	2.1	21.38	29.04	20.9
α-Pyrrolidin carboxylic acid	3.1	5.1	1.74	2.34	1.7
Phenylalanin	3.2	0.4	3.89	4.24	2.4
Glutamic acid	10.7	0.88	0.76	1.73	6.3
Aspartic acid	1.2	0.56	....	4.43	4.5
Cystin	0.065	....	1.0	0.31	0.25
Serin	0.23	....	....	0.56	0.33
Oxy-α-Pyrrolidin carboxylic acid	0.25	3.0	....	1.04	2.0
Tyrosin	4.5	....	0.34	1.33	2.13
Amino-valerianic acid	1.0	....	....	....	*
Lysin	5.80	2.75	....	4.28	2.0
Histidin	2.59	7.62	....	10.90	1.0
Arginin	4.84	0.40	0.3	5.42	11.7
Tryptophan	1.5	....	....	*	*

* Present.

B. THE COMPOUND PROTEIDS

Simple proteids are distinguished largely by the fact that they can unite with each other as well as with other substances to form new compounds. The atomic group conjoined with the proteid in the latter case is described by Kossel as the *prosthetic* group. Such conjugated proteids can be isolated from the animal fluids and tissues in great numbers. They are classified according to the nature of the conjugant into the following groups:

A. *Hæmoglobins:* These represent compounds of a basic proteid body, globin, with the acid, iron-containing, pigment hæmochromogen, and will be discussed at length in Chapter V.

B. *Nucleo-albumins:* phosphorus-containing proteids which are characterized by the fact that on digestion with pepsin-HCl a portion remains temporarily insoluble. This portion, like the soluble portion, contains phosphorus, and is described as pseudonuclein or paranuclein. It is distinguished from the true nucleins (see below) by not containing any purin bases.

To the nucleo-albumins belong the casein of milk, whose properties will be fully considered later (Chapter XXVI); vitellin found in the yolk of a bird's egg; various proteids of the bile, the kidneys, the mucous membrane of the bladder, etc.

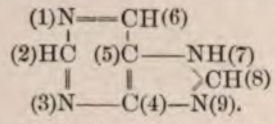
Little is known yet with regard to the constitution of paranuclein, or the form in which phosphorus is found either in it or in the nucleo-albumins in general. Levene and Alsberg however have isolated an acid (vitellinic acid) from vitellin which possibly represents a compound of proteid with phosphoric acid in the form of an ester. Like the corresponding pseudonuclein this acid contains iron in organic combination, which, as Bunge believes, may serve for the formation of the iron-containing hæmoglobin of the young bird. Likewise from casein a paranucleinic acid has been obtained by Salkowski, from which orthophosphoric acid can be split off.

Neither casein nor vitellin contains any carbohydrate group. Twenty-seven and one-tenth per cent of the total nitrogen in cow's-milk casein occurs as diamino-N, and sixty-two per cent as monamino-N. The maximal yield of tyrosin from casein is 4.5 per cent. Only about one-tenth of the sulphur of casein is present in the form of cystin compounds (Mörner).

C. *Nucleins:* compounds of proteid with the nucleic acids.

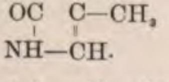
The nucleic acids are phosphorus-containing substances which yield on decomposition, besides phosphoric or metaphosphoric acid: different characteristic purin bases; the pyrimidin derivatives thymin, uracil, and cytosin; and finally carbohydrates. Moreover they are dextro-rotatory, notwithstanding that nucleins and even the nucleo-proteids (see below) are lævo-rotatory.

1. *The purin bases* (called also alloxuric, xanthin, or nuclein bases) are derivatives of purin, which, according to Fischer, consists of a pyrimidin nucleus and a glyoxalin nucleus joined to the former in the 4, 5 position,



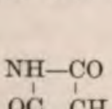
Different hydrogen atoms of this structure may be replaced by hydroxyl, amid, or alkyl groups. The purin bases are: xanthin (2.6.dioxypurin, $C_5H_4N_4O_2$); guanin (2.amino-6.oxypurin, $C_5H_5N_5O$); hypoxanthin (6.oxypurin, $C_5H_4N_4O$); and adenin (6.amino-purin, $C_5H_5N_5$). In guanylic acid from the pancreas only guanin is found. Several purin bases occur in the other nucleic acids and in the nucleic acid from yeast all of them are found.

2. *Thymin,* discovered by Kossel in the nucleic acid of the thymus, is 5.methyl-2.6.dioxy-pyrimidin,



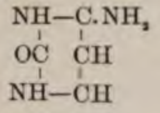
It has been found also in the nucleic acids of the spleen, of fish sperm, of the brain, liver and pancreas.

3. *Uracil,* 2.6-dioxy-pyrimidin,



occurs in the nucleic acid of yeast and in those of the pancreas, thymus, herring sperm, etc. (Ascoli).

4. *Cytosin*, 6.amino-2.oxy-pyrimidin,

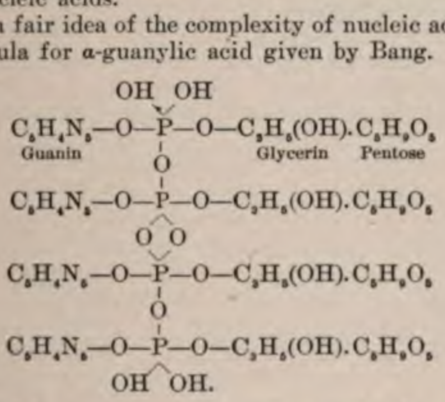


(Kossel) has an equally wide distribution.

5. In nearly all of the nucleic acids there is a *carbohydrate*, sometimes a pentose (l-xylose), sometimes a hexose.

Nothing definite is known concerning the manner in which phosphorus is combined in the nucleic acids.

One can obtain a fair idea of the complexity of nucleic acids from the following structural formula for α-guanylic acid given by Bang.



The simplest nucleins are the saltlike compounds of nucleic acids with the protamins and histons. These simple proteids are closely related chemically, and there seems to be a close relationship physiologically as well; for whereas one finds histons in unripe fish sperm, in the ripe sperm protamins are found.

The nucleins finally unite with proteid to form *nucleo-proteids*, which, it appears, occur in (dead) cell protoplasm and especially in the (dead) cell nucleus, where Miescher first demonstrated them. Their composition is very complicated, and they represent the first decomposition products of the living substance thus far known. Some of them appear to contain iron.

D. *Chondro-proteids*. Compounds of proteid with chondroïtin-sulphuric acid ($C_{18}H_{27}NSO_{17}$ Schmiedeberg) and found in the mucoid of cartilage, amyloid, in tendon mucin, and presumably in other mucous substances.

C. SUBSTANCES RESEMBLING PROTEIDS

The following substances are known to be closely related to proteids, from the fact that on decomposition they yield in general the same substances as do proteids. It is possible that some of them should be enumerated among the true proteids.

A. *Protamins* (see page 70).

B. *Keratin*, a substance rich in sulphur (2.5–5 per cent); amorphous, insoluble in water, alcohol, ether and the digestive fluids; contained in horn, epidermis, hair, nails, etc. On heating with water in closed tubes it yields albumoses and peptones. It develops the characteristic smell of burnt horn when ignited.

About the same products (with the exception of carbohydrates) have been obtained by cleavage of the keratin molecule, as from the typical proteids.

C. *Albumoid*, a substance obtained from the cartilage of the trachea, which stands in certain respects between the true proteid and keratin. Another albumoid occurs in the fibers of the crystalline lens.

D. *Elastin*, a yellowish white, amorphous substance containing only a small quantity of sulphur; insoluble in water, alcohol and ether; and attacked by chemical reagents with great difficulty. It occurs in connective tissue and especially in the ligamentum nuchæ.

Among the cleavage products of proteid which have been obtained from elastin, are the guanidin rest, leucin, diamino acids, tyrosin and indol, but neither glutamic acid nor carbohydrates.

E. *Collagen*, a sulphur-containing substance; insoluble in water, salt solutions, and very weak acids and bases, but swelling up in less dilute acids; it is the chief constituent of fibrillar connective tissue and occurs in bone (osseïn) and other tissues.

When collagen is boiled for a long time with water, it passes over into gelatin (glutin).

F. *Gelatin*, a colorless, amorphous, nondiffusible substance of about the same chemical constitution as collagen. It swells up in cold water and is dissolved in warm water. On cooling the solution sets into a jellylike mass.

Neither carbohydrates, cystin, serin, tyrosin, nor indol occurs in the molecule of gelatin. Sixteen and six-tenths per cent of the total nitrogen is present as arginin, and not less than 8.4 per cent in the form of glycocoll.

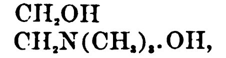
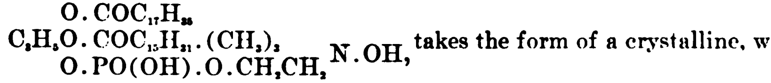
Gelatin solutions are not coagulated on boiling, and are not precipitated by mineral acids, acetic acid, alum, lead acetate or metallic salts. They are precipitated by tannic acid in the presence of salt, by acetic acid and NaCl in substance, by mercuric chloride in the presence of HCl and NaCl.

By prolonged cooking gelatin is transformed into a nongelatinizing modification. It is acted upon by the digestive enzymes yielding gelatin albumoses and peptones.

G. *Reticulin*, a constituent of the connective tissue framework, of the lymph glands, of the spleen, of the intestinal mucosa, the liver, kidneys and alveoli of the lungs.

D. OTHER NITROGENOUS SUBSTANCES

Among the remaining nitrogenous substances which may be isolated from animal tissues, *lecithin* should be especially mentioned. It is found in almost all animal and plant cells, especially in the brain, the nerves, the blood corpuscles and in egg yolk; it occurs also in almost all animal fluids.

Lecithin represents an esterlike compound of a base, cholin, oxyethyl-trimethyl-ammonium-hydroxide,  $\begin{array}{l} CH_2OH \\ CH_2N(CH_3)_3.OH \end{array}$, with glycerin-phosphoric acid which is united with two fatty acid radicles into a glyceride. There are different lecithins therefore according to the kind of the fatty acid radicles. The stearic-palmitic acid lecithin to be obtained from egg yolk,  $C_3H_5\begin{array}{l} O.COC_{17}H_{35} \\ O.COC_{15}H_{31} \\ O.PO(OH).O.CH_2CH_2 \end{array}\!\!\!\begin{array}{l} (CH_3)_3 \\ \\ \end{array} N.OH$, takes the form of a crystalline, waxlike mass readily soluble in alcohol and ether. With water it swells up forming an opalescent solution, from which it is precipitated again by means of different salts.

Lecithin is found in several cases in loose combination with proteid or other substances. In *protagon* which occurs in the white substance of the central nervous system, and probably represents a mixture of substances, lecithin is bound up with the *cerebrosides*, N-containing, phosphorus-free substances, which on boiling with dilute mineral acids yield a reducing sugar. *Ovovitillin* is a combination of proteid and lecithin, and similar compounds are said to be obtained as insoluble residues from peptic digestion of the gastric mucosa, liver, kidneys, etc. These *lecithin albumins* represent therefore a new group of proteids (cf. under B). *Jecorin*, which has been demonstrated in the liver and in the blood, is a combination of lecithin and glucose.

§ 2. THE NONNITROGENOUS SUBSTANCES

A. FATS

The fats are esters of the triatomic alcohols, the glycerins, with monobasic fatty acids, chief of which in the animal fats are: *stearic acid*, $C_{18}H_{36}O_2$, *palmitic acid*, $C_{16}H_{32}O_2$, and *oleic acid*, $C_{18}H_{34}O_2$. The triglycerides of the first two—*stearin*, $C_3H_5.(C_{18}H_{35}O_2)_3$, and *palmitin*, $C_3H_5.(C_{16}H_{31}O_2)_3$—melt only at a temperature far above that of the body. The glyceride of oleic acid, *olein*, $C_3H_5.(C_{18}H_{33}O_2)_3$, is on the other hand fluid at ordinary temperatures and solidifies in the form of crystalline needles only at $-5°$ C. The melting point of a mixture of the three glycerides must therefore depend upon the relative content of olein—the greater the relative quantity of this fat, the lower is the melting point of the mixture. Moreover the melting point of fat shows considerable variation not only in different species of animals, but also in different parts of the same individual, which means that the relative quantity of olein present varies considerably. Traces of fatty acids are also found in animal fat.

The following reactions, among others, serve to distinguish the different fats: (1) the *acid equivalent*, which is the measure of the content of free acid in a fat, and is obtained by titration of the fat dissolved in alcohol ether with n/10 alcoholic caustic potash; (2) The *saponification equivalent*—i. e., the number of mg. of KOH combined with fatty acid in saponification of 1 g. of the fat with alcoholic caustic potash; (3) The *Reichert-Meissl equivalent*, which gives the amount of volatile fatty acid obtained, when, after saponification, the fat is distilled off in the presence of a mineral acid; (4) The *iodine equivalent*—i. e., the quantity of iodine taken up by a fat, and serving as the measure of the content of olein.

In the body fat is to be found for the most part inclosed in the cells of the fatty tissues. These represent in fact a kind of storehouse for fats (cf. Chapter IV). It occurs also in very small quantities in the blood and in other fluids of the body.

Fats are insoluble in water, are dissolved by boiling-hot alcohol, but are precipitated again on cooling. They are readily soluble in ether, benzol and chloroform. On boiling with caustic alkalies they are decomposed and are split into glycerin and fatty acids, the latter of which unite with the alkali to form soap. The fatty acids are set free from the soap by strong acids. Like the neutral fats they are soluble in ether, but this is not the case with soaps.

B. CHOLESTERIN

Cholesterin is a monatomic alcohol, $C_{27}H_{45}OH$, which occurs especially in certain biliary concretions, also in the brain, in nerves and in animal cells generally. From an alcoholic solution it crystallizes in the form of leaflets which have the appearance of mother-of-pearl. With the higher fatty acids cholesterin forms esters, which, unlike the fats, are very resistant toward decomposing reagents and are therefore specially suitable for protection to the skin, being found on both hair and feathers. *Lanolin*, a compound of this kind prepared from wool fat, has found wide practical use.

C. CARBOHYDRATES

The name carbohydrates is applied to substances composed of C, H, and O, in which the H and O are present in the proportions to form water. This definition however is not sufficient, for there are substances with the same relative quantities of H and O which are not carbohydrates; and for other reasons it cannot be regarded as satisfactory from a scientific point of view. A perfectly satisfactory definition of carbohydrates has not yet been given; they are characterized only as *aldehyde or ketone derivatives of polyhydric alcohols.*

The carbohydrates are divided into three chief groups, namely, monosaccharides, disaccharides and polysaccharides, in each of which are found several familiar substances.

A. The *monosaccharides* are the direct, isomeric or stereo-isomeric aldehydes or ketones of the corresponding alcohols. They occur ready formed in nature, and have also been prepared synthetically.

The monosaccharides most interesting to us in this connection are the *hexoses*, $C_6H_{12}O_6$: dextrose, mannose, galactose, and levulose, which are the first oxidation products of the stereo-isomeric hexatomic alcohols: sorbite, mannite, and dulcite. The latter have the following constitution: $CH_2.OH.(CH.OH)_4.CH_2.OH$. Dextrose, mannose, and galactose are the respective aldehydes of these alcohols, $CH_2.OH.(CH.OH)_4.CHO$; levulose is the ketone of mannite, $CH_2.OH.(CH.OH)_3.CO.CH_2OH$.

The following reactions are common for all these substances: They are directly fermentable, and under the influence of the yeast plant are decomposed into CO_2 and alcohol: $C_6H_{12}O_6 = 2C_2H_5.OH + 2CO_2$. They are easily oxidized and hence reduce the metallic oxides on heating in alkaline fluids. This property is made use of in quantitative determinations of the monosaccharides. They are for the most part crystalline substances of a sweetish taste; readily soluble in water, difficultly soluble in alcohol. The hexoses occurring in nature, in solutions rotate the plane of polarized light either to the right or to the left. This property also is valuable for their quantitative determination.

1. *Dextrose* (synonyms: grape sugar, glucose) occurs in sweet fruits (e. g., grapes) and in honey. Under normal circumstances dextrose is found in small quantities in the blood and lymph. In diabetes its quantity in these fluids is greater, and it is found in large quantities in the urine. Dextrose rotates the plane of polarized light to the right.

2. *Levulose* (synonyms: fruit sugar, fructose) occurs together with dextrose in sweet fruits and in honey. It rotates the plane of polarized light to the left.

Of the other monosaccharides the *pentoses*, $C_5H_{10}O_5$, have been demonstrated in animal fluids (urine) and among the cleavage products of animal substances. *Arabinose*, found in the urine, and *xylose* in the pancreas are the most important pentoses. They do not ferment under the influence of the yeast plant; but with a certain other fungus, not definitely determined, Salkowsky obtained a large quantity of alcohol from l-arabinose.

B. *The disaccharides* are anhydric compounds of two molecules of monosaccharides—e. g., $2C_6H_{12}O_6 = C_{12}H_{22}O_{11} + H_2O$. On boiling with dilute mineral acids they break up with the absorption of water into monosaccharides. The most important members of this group are saccharose (cane sugar), lactose (milk sugar) and maltose (malt sugar), all having the formula $C_{12}H_{22}O_{11}$.

The disaccharides are crystalline bodies of a sweetish taste, readily soluble in water. Lactose and maltose reduce an alkaline copper solution, saccharose does not. By boiling with dilute mineral acids and by the agency of certain enzymes the disaccharides take up one molecule of water and split into two molecules of monosaccharides thus: saccharose into dextrose and levulose; lactose into dextrose and galactose; maltose into two molecules of dextrose.

Saccharose is dextro-rotatory; on its cleavage into dextrose and levulose it becomes, on account of the stronger rotating power of levulose, lævo-rotatory. For this reason the cleavage of saccharose is called *inversion*.

C. The *polysaccharides*, $n(C_6H_{10}O_5)$, like the disaccharides are regarded as anhydrides of the monosaccharides, but they have their origin in the union of many molecules of the latter and have a high molecular weight, which varies widely.

The polysaccharides have no sweetish taste and for the most part are amorphous. Some are soluble in water, others swell up in water, while still other members of this series are not visibly changed by water. By various means all of them can be transformed by absorption of water into monosaccharides.

The polysaccharides are divided into three chief groups: starches, gums, and cellulose.

1. The *starches* are not directly fermentable and do not reduce alkaline copper solutions. To these belong:

(*a*) *Vegetable starches* (amylum). These are found in many plant cells laid down in the form of microscopic, round or oblong granules which have an organic structure and are insoluble in cold water. On heating with water they swell up at 50°, burst and partially dissolve, forming a slimy solution, known as *starch paste*, which can be filtered. The soluble part is called *starch granulose*, the insoluble part *starch cellulose*. On boiling with dilute acids starch is changed first into dextrin (see below) and later into dextrose. By digestion with saliva or pancreatic juice, or through the influence of malt-diastase it is split into dextrin and maltose (cf. Chapter VII).

(*b*) *Glycogen* is an animal starch which has a very wide distribution in the animal body. It is found in almost all the tissues of the body, but in largest quantities in the liver and in the muscles; it is a constituent of embryonic tissues especially and all others in which an active cell formation is taking place. Glycogen is an amorphous, tasteless and odorless white powder; with water it forms an opalescent, dextro-rotatory solution. It is changed by diastatic enzymes into maltose or dextrose according to the nature of the enzyme.

2. *Gums* are amorphous, transparent, tasteless and odorless substances which with cold water form viscous fluids. They are very widely distributed in the plant kingdom.

(*a*) Among the gums the *dextrins* claim our chief interest here, for they are formed as intermediate products in the transformation of starch in the alimentary canal. They are obtained also by heating starch up to 200°–210° C. In these transformations of starch a series of dextrins is formed which have smaller and smaller molecular weights. The dextrins are white or yellowish white, amorphous, gumlike masses whose aqueous solutions are dextro-rotatory. They are not directly fermentable.

(*b*) An *animal gum* is said to be split off from mucin through the influence of superheated steam and of alkalies. This is not true, however, for all mucins, for several kinds yield gumlike substances which represent nitrogenous bodies derived from the carbohydrates.

3. *Cellulose* forms the chief constituent of the cell walls of all plants and exhibits an organic structure. To obtain pure cellulose plant fibers are digested successively with different reagents, such as dilute acids and alkalies, potassium chlorate and nitric acid, alcohol and ether. The cellulose remains as the insoluble residue.

Table showing the percentage composition of the most important substances discussed in this chapter:

	C	H	N	S	O	P
1. Proteids in general.	50.6–55	6.5–7.7	15.0–18.5	0.3–2.2	20.5–23.5	......
2. Casein	52.7–54.0	7.0	15.6–15.7	0.7–0.8	22.8	0.8
3. Nuclein	40.8–42.1	5.4–6.1	14.7–16.0	0.4–0.6	31.1–31.3	5.2–6.2
4. Nucleic acid.......	34.1–37.3	4.2–5.2	15.3–18.2	......	32.5–35.6	7.7–9.9
5. Nucleohiston......	48.5	7.0	16.9	0.7	24.0	3.0
6. Mucin.............	48.3–50.3	6.4–8.2	11.8–13.7	0.8–1.8	27.4–32.7	......
7. Chondromucoid ...	47.3	6.4	12.6	2.4	31.3	......
8. Keratin............	49.8–58.5	6.4–8.2	11.5–17.5	2.5–5.0	19.6–22.9	......
9. Elastin	54.0–54.3	7.0–7.3	16.7–16.8	0.4	21.8–21.9	......
10. Collagen..........	50.8	6.5	17.9	0.6	24.3	......
11. Gelatin	49.3–51.5	6.5–7.1	17.5–18.6	0.3	25.2–25.4	......
12. Reticulin	52.9	7.0	15.6	1.9	20.0	0.3
13. Lecithin..........	65.4	11.2	1.7	......	17.8	3.8
14. Fats (mean).......	76.5	12.2	......	......	11.5	......
15. Cholesterin	83.9	11.9	......	......	4.1	......
16. Monosaccharides...	40.0	6.7	......	......	53.3	......
17. Disaccharides	42.1	6.4	......	......	51.5	......
18. Polysaccharides....	44.4	6.1	......	......	49.4	......

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CHAPTER IV

METABOLISM AND NUTRITION

THE physiology of metabolism and nutrition[1] seeks to discover what substances are necessary for the maintenance and growth of the body, to determine the character and extent of the combustion taking place in its tissues and fluids under different circumstances, and to understand the significance of the different substances for these processes.

The substances in question admit of division into three groups, namely: (1) *organic foodstuffs*, substances which supply potential energy and serve therefore to maintain the combustion in the body; (2) *water and inorganic foodstuffs*, which must be taken to make good the constant loss from the body of these constituents, without which profound and eventually fatal disturbances in health may ensue; (3) *oxygen* necessary for the maintenance of combustion.

FIRST SECTION

METABOLISM

§ 1. ON THE METHOD OF METABOLISM EXPERIMENTS

A. THE INGESTA

Organic as well as *inorganic foodstuffs*, mixed together in varying proportions and mixed with other substances not needed in the body, occur in our common articles of food and in our meals prepared from them. Chemical analysis of the foods has shown that the organic foodstuffs are chiefly of three kinds, namely: (1) *proteids* and allied substances; (2) *fats*; (3) *carbohydrates*. To the inorganic foodstuffs, which are designated also as *ash constituents*, belong numerous salts which we shall discuss more in detail later. By chemical analysis of the food we learn its composition, both qualitatively and quantitatively, and determine in this way precisely the intake of the body.

In analysis of the foods and the fæces, (1) the *nitrogen* is determined and the proteid is calculated by multiplying this result by 6.25. Since, however, nitrogen-containing substances other than proteid occur in both animal and vegetable foods, the quantity as calculated by this method is too high. Especially with a low percentage of proteid a considerable error might thus arise. Moreover, the kind of proteid eaten is not a matter of indifference, since one may well imagine that different proteid bodies behave differently in metabolism. The little we know on this subject will be summarized later. (2) As *fat*, is reckoned the total extract with ether, although this contains also other substances soluble in ether. (3) The *dry substance* and (4) the *ash constituents* are determined by desiccation at 100° C. and by incineration respectively. (5) The *carbohydrates* are determined usually by subtracting from the total dry substance the proteid + the fat + the ash.

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[1] It may serve to differentiate the two divisions of the subject somewhat, if we define metabolism as covering all those chemical transformations of the foodstuffs by which *energy* is supplied to the cells, and nutrition as covering all the processes by which the *materials* which the cells require are supplied. Obviously the two are inseparable and represent merely different aspects of the same subject. We speak of the substances as *undergoing* metabolism and of the organism as *nourishing* itself.—ED.

Finally, under the ingesta is to be reckoned the oxygen, methods for the determination of which will be given under B.

B. DETERMINATION OF THE EXCRETA

The products of metabolism are eliminated by the lungs, skin, intestine and kidneys.

The excreta resulting from the combustion of organic foods, to which we shall confine ourselves for the present, contain the following elements: N, S, P, C, H, and O. Nitrogen, sulphur and phosphorus are derived from proteids; carbon, hydrogen and oxygen are contained in all the organic foods. In estimating the excreta we have therefore to determine quantitatively the amount of N, S, P, C, and H eliminated within a certain time.

The determinations can be simplified considerably, however. Ordinarily, in order to find out how much proteid has been metabolized in the body, it is sufficient to determine the amount of nitrogen eliminated. One need not consider the sulphur and phosphorus unless the investigation is especially concerned with the behavior of the phosphorus-containing proteids. The analysis for a complete metabolism experiment therefore can be restricted to N, C, and H. Commonly the excretion of hydrogen also is neglected.

The amount of proteid destroyed in the body is obtained by multiplying the amount of nitrogen eliminated as a product of metabolism by 6.25.

Analysis for the elements found in the excreta is by no means always sufficient; in many cases it is necessary either for the purpose of gaining a deeper insight into the mode of the metabolic processes, or in order to estimate the percentage of combustible materials in the fæces, to determine the separate compounds quantitatively. In the latter case the analysis is carried out in precisely the same way as in making similar determinations for the food to be ingested.

If the metabolism experiment is to be of any use whatever, it is necessary to collect *every trace of the excreta* for exactly the period covered by the experiment. The urine and the fæces offer no particular difficulties in this respect, although some remarks with regard to the latter seem called for.

It is apparent at once that analysis of the fæces can only be of importance for the study of metabolism, if they can be identified as belonging to a definite diet. But in all animals, as in man, the intestine is always more or less filled and one cannot tell without special means whether a given mass of fæces comes from the diet which is being studied. To do so it is necessary to separate the fæces corresponding to the diet in question from preceding and subsequent fæces. The subject is allowed to fast for some twenty hours, then the particular diet is begun, and with the first meal some substance is given which, like finely powdered charcoal, will impart a characteristic color to the fæces. After the last meal the subject is permitted to fast again for twenty hours, and with the first food eaten after this period charcoal is once more given. With herbivorous animals it is impossible to get a satisfactory separation; but this difficulty may be overcome by giving the particular diet under investigation for several days before beginning the experiment.

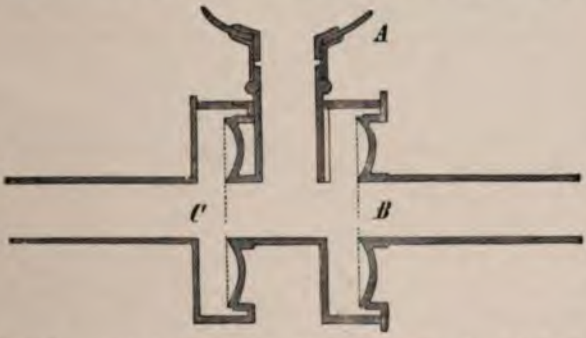

FIG. 39.—Face mask for respiration experiments, after Lovén. Longitudinal section. A, the mouthpiece. B and C are thin membranes which act as valves and serve to separate inspired from expired air. Inspiration takes place through B, expiration through C.

In order to collect the solid constituents contained in the sweat, the subject is required to wear thoroughly washed woolen clothes which will absorb and retain all such solids.

Rather complicated methods must be employed to collect and analyze the gaseous products of metabolism (carbon dioxide and water vapor), and to determine the amount of oxygen absorbed. Methods for all these purposes were used by Lavoisier (1780), but they have been developed and improved in many ways since his day.

The simplest, if not the most satisfactory method, is to collect the respiratory products by the use of a *face mask*. The mask is connected by means of tubes with apparatus for the measurement and collection of the inspired and expired air, the two currents of air being separated by means of automatic valves (Fig. 39). Instead of the face mask a gutta-percha plate, so arranged as to fit between the lips and teeth and provided with a tube through which the air passes, may also be used. A much more nearly air-tight closure of the mouth is possible with this apparatus.

By this method which has recently been improved, especially by Zuntz, the cutaneous respiration is of course not determined, but it is of no particular importance (cf. Chapter XIII). A more serious objection is, that with this method it is very difficult, if not impossible, to continue the experiment for more than a quarter of an hour to an hour. Where it is necessary to determine the CO_2 and water excreted and the oxygen absorbed for a whole day or longer, other methods must be used.

For these purposes several different forms of respiration apparatus have been constructed, among which we shall very briefly describe the following:

1. [*The Apparatus of Atwater and Benedict.*—In its general features this apparatus, constructed for experiments on human subjects, embodies the principles of one originally constructed by Regnault and Rieset (1849) for experiments on smaller animals. The subject is placed in a respiration chamber of suitable size (5.03 cubic meters capacity) and is supplied with pure air, as indicated in the diagram below (Fig. 40). The air containing the respiratory products is drawn out of the chamber by the pump and is made to pass in turn over H_2SO_4 and soda lime. The gain in weight of the former gives the amount of water eliminated by the respiration and evaporation; the gain in weight of the latter, the amount of carbon dioxide eliminated. Pure oxygen is next admitted to make up what has been taken out by the subject. To determine exactly how much oxygen has been thus absorbed it is necessary to know how much was contained in the air at the beginning and how much at the end of the experiment. Subtracting the amount present at the end from the total amount supplied—i. e., the amount present at the beginning plus the amount admitted—gives directly the amount absorbed.

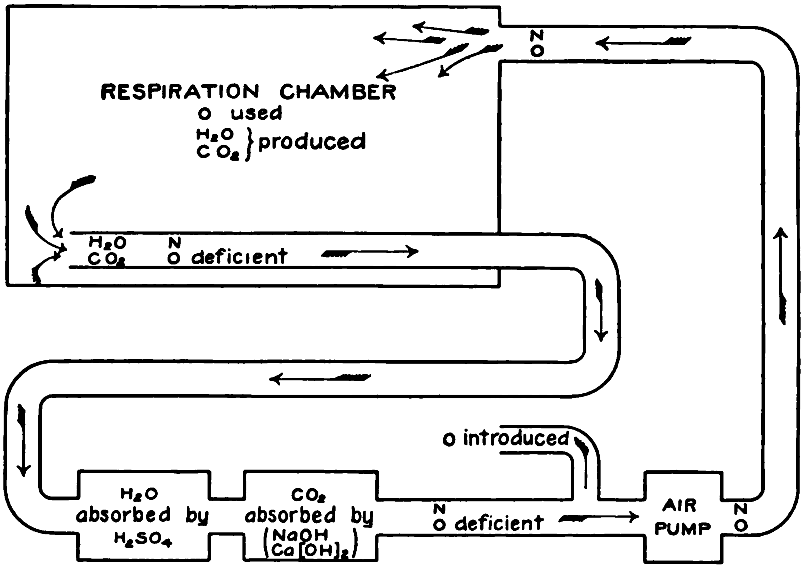

FIG. 40.—Schema of the Atwater-Benedict respiration calorimeter.

The respiration chamber in this apparatus is provided also with means of measuring the heat lost from the subject's body by radiation and conduction, so that the entire apparatus is described as a respiration calorimeter.—ED.]

2. *The Apparatus of Pettenkoffer.*—This consists of a respiration chamber with a capacity of 12.7 cubic meters into which and from which air is pumped in a continuous stream. The air is analyzed both as it goes in and as it comes out of the chamber, a uniform fractional part of the total volume flowing out

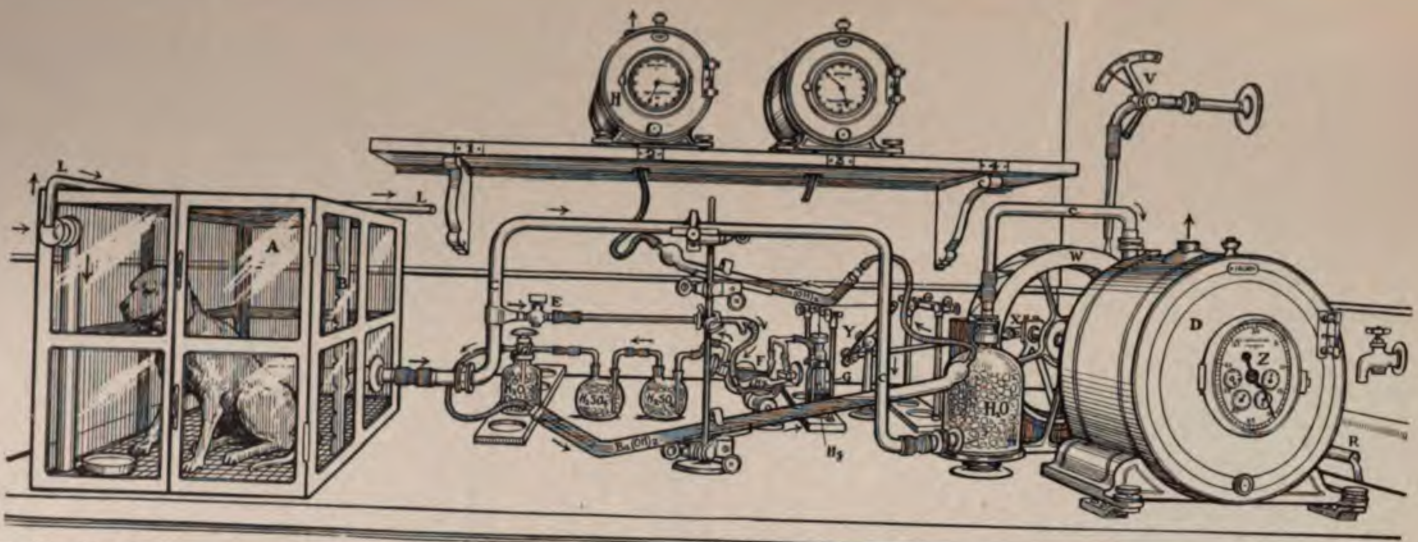

FIG. 41.—The smaller respiration apparatus of Pettenkoffer and Voit. Air enters the cage, A, at the upper left-hand corner. It is drawn out through openings in the tube B (so spaced as to insure thorough diffusion) through the tube, C, and the large H_2O flask, where it is saturated with moisture, to the gas meter, D, where it is measured. The meter is driven by a water wheel, W, rotated at a uniform rate of speed by a constant head of water pressure, V. At E a side tube leads off from C conveying a sample of cage air for analysis. This air is drawn through a mercury valve, F, by means of the mercury pump, G. The latter is operated by the mechanism, X, Y, connected with the water wheel. From the valve F, this air passes through two H_2SO_4 flasks and is then saturated with moisture so as to prevent loss of water from the $Ba(OH)_2$ tubes. Of course, the air, as it leaves the $Ba(OH)_2$ tubes, is saturated with moisture, and is measured by the small gas meter, H, just as in the case of the large meter, while in this saturated condition. A duplicate sample is led off at the same time through another branch of the tube, E, and through another system of vessels to the gas meter at 3. Through the branches of the tube, L, duplicate samples of the air which enters the cage are drawn in the same manner to similar valves, and then through similar vessels and tubes to meters placed at 1 and 4.

being led off to suitable apparatus for the absorption of carbon dioxide and water.

[A smaller apparatus embodying the same principles has been constructed by Voit for experiments on smaller animals (Fig. 41). The cage (A) is ventilated by a current of air kept moving by rotation of the gas meter (D). Throughout the experiment a sample of this air is continually led off by a side tube (E) and is passed over pumice stone soaked in sulphuric acid and then through $Ba(OH)_2$. The quantity of H_2O in this air is obtained directly by the difference in the weight of the H_2SO_4 flasks,[1] the amount of CO_2 by titration of the $Ba(OH)_2$. The large gas meter (D) measures the total volume of air passing through its works, and the small gas meter (H) measures the volume of the sample. A duplicate analysis is made by means of a second set of vessels, and this sample is measured by a similar gas meter. Duplicate analyses of the air which enters the cage are made in the same manner and the respiratory products calculated by difference.

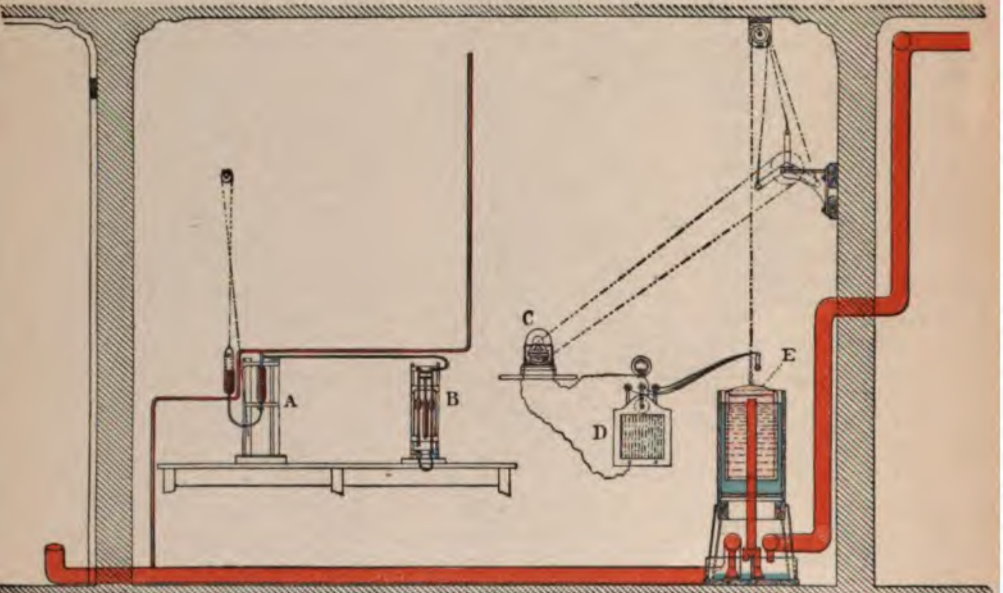

FIG. 42.—The respiration apparatus of Sondén and Tigerstedt. A, container for sample of the room air; B, apparatus for determination of CO_2; C, electric motor; D, rheostat; E, hydraulic pump.

If the determination of water vapor is satisfactory, the amount of oxygen absorbed by the animal can be obtained by subtracting the combined weight of the animal at the beginning of the experiment and the total ingesta for the period from the combined weight of the animal at the end and the total excreta for the period.—Ed.]

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[1] Voit and Pettenkoffer made very thorough tests of this method, and found that the water is obtained to within 1 or 2 per cent, the slight error being due to condensation on the walls of the tubes. Rubner, employing the same principles of ventilation for his calorimeter, obtained still more exact results. By shortening the distance which the air must travel on its way from the cage to the H_2SO_4 flasks, he was able to prevent entirely the condensation of water on the walls of the tubes. For short experiments he relied upon hair hydrometers placed inside the cage.—ED.

3. *The Apparatus of Sondén and Tigerstedt* (Fig. 42).—The subject is housed in an ordinary room with a capacity of 100.6 cu.m. The walls, ceiling, and floors are covered with sheet zinc and are made air-tight by soldering all the joints. By means of a hydraulic pump (E) air is drawn from this respiration chamber to a gas meter, where it is measured. Fresh air from outdoors replaces the foul air drawn out. A uniform diffusion of the air in the room is insured by a ventilating fan.

To obtain air for analysis, a narrow tube branches off from the main inlet pipe (red), and by means of another hydraulic pump a constant stream is maintained through it, so that the air in the branch always has the same composition as that in the main inlet. At stated intervals samples for analysis are then taken (in the vessel A) from this branch and the carbon dioxide is estimated by the method of Pettersson (B) for the analysis of gases. The quantity of carbon dioxide is calculated by the ventilation formula of Lenz.

But the body suffers other losses in organic substance than those resulting from combustion. Here belong the losses by sloughing off of the epidermis, cutting the hair and nails, ejection of sperm and menstrual blood, secretion of milk, etc. Such losses, however, are either so slight that they do not affect the results of the investigation, or they come in only occasionally and can generally be neglected, unless the investigation is being directed especially to them.

C. APPORTIONMENT OF THE INDIVIDUAL ELEMENTS TO THE DIFFERENT EXCRETA

(1) *Expired Air.*—It has been known since the beginning of scientific investigation of metabolism and can be demonstrated without the least difficulty that carbon and hydrogen leave the body as CO_2 and H_2O in the expired air. Not so with the nitrogen and nitrogenous compounds. *A priori* one cannot deny that such substances also might be given off from the body as products of metabolism in the expired air. But from the many researches which have been carried out with reference to this question, it appears certain that this is not the case. So far as metabolism is concerned we need, therefore, to consider among the respiratory products only carbon dioxide and water vapor.

(2) *Sweat.*—Water is the principal substance given off through the skin. However, the sweat contains also some solid substances, the most important of which is urea. With copious sweating, as under severe labor or in a vapor bath, the quantity of these constituents may rise so much that to neglect them would involve considerable error. Thus, under such circumstances, 0.76 g. N have been found in the sweat; at the same time the nitrogen excretion in the urine was 15.9 g. for twenty-four hours. In this case, therefore, the sweat contained 4.8 per cent of the N eliminated through the kidneys (Argutinsky).

(3) *Urine.*—Of the chemical elements derived from the organic foodstuffs and found in the urine, nitrogen and carbon are to be specially considered. Both of these occur mainly in the form of urea and uric acid. The daily quantity of nitrogen eliminated in the urine of an adult man amounts

to about 15–16 g., but exhibits wide variations, depending primarily upon the quantity of nitrogen ingested in the food.

The quantity of carbon in the urine as compared with that in the expired air is very small. Only when very great exactness is desired does it need to be determined directly, for it can generally be calculated without any considerable error from the nitrogen of the urine. The ratio N:C in the urine exhibits but very slight variations; according to Atwater, it has for a mixed diet a mean value of about 1:0.72 (0.64–0.79).

(4) *Fæces.*—The fæces are composed partly of unabsorbed residues of the food, partly of residues of the digestive fluids, and partly of worn-out epithelial cells and excretory products from the alimentary tract. In a fasting man these residues make up a fæcal mass, which contains from 0.11 to 0.32 g. of nitrogen per twenty-four hours. When a nonnitrogenous diet, or one very poor in nitrogen, is given, from 0.5 to 0.4 g. of N appear in the fæces per day (Rubner, Rieder). This quantity of N must evidently have its origin in the intestine itself. We can say, therefore, that the intestine has a very large share in the formation of the fæces, and that in round numbers one gram of the N eliminated as a product of metabolism is to be found in the intestinal evacuations. The nitrogen contained in the bacteria of the fæces is also included in this figure.

Since experiments from Pawlow's laboratory (Chapter VII) show that the secretion of the digestive juices and their N-content present considerable variations with different diets, one might be tempted to look upon the total quantity of nitrogen in the fæces as a pure product of metabolism. But this is not true, for many observations have shown that with certain articles of diet a considerable part of this fæcal nitrogen actually represents a residue of the food.

In any given case therefore it is quite impossible to decide how much of the fæcal nitrogen comes from the one source and how much from the other. For this reason it has become customary to regard the total nitrogen in the fæces as a residue of the food. Although it must be admitted that such an assumption is quite incorrect from a purely theoretical point of view, it makes no difference in the calculation of results of metabolism experiments. For if we suppose that the fæces are exclusively a product of metabolism, the implication is that all the food was absorbed without loss; and *vice versa*, if we regard the fæces as only a residue of the food, then the quantity utilized must be diminished by the mass of the fæces. In both cases we reach exactly the same result with regard to the amount of metabolism actually taking place. In this presentation of the subject of metabolism, therefore, we shall reckon the fæces as a residue of the food.

Respecting the *nonnitrogenous substances* given off in the fæces, we may merely mention here the fact that fat occurs in appreciable quantity both on a fat-free diet and in fasting. In the latter case 0.6–1.4 g. per day have been found in the fæces, and on a fat-free diet, 3–7 g. per day. If, therefore, on a fat diet the fæces do not contain more than 7 g. of fat per day, we can say that the fat in the food has been almost entirely absorbed in the intestine.

In the fæces the ratio of N:C for a mixed diet is about 1:9.2 (6.8–13.8). Inasmuch as the quantity of nitrogen in the fæces ordinarily does not amount to more than 2 g. per day, in most cases it is sufficient to calculate the carbon from the nitrogen.

We have already seen that under normal circumstances no nitrogen is eliminated in the expired air as a product of metabolism, and that in the sweat only in exceptional cases is the quantity of any importance. Hence the channels by which nitrogen is excreted are the kidneys and the intestine as will appear plainly from a case of *nitrogenous equilibrium.*

If an animal be given a diet, which from day to day contains exactly the same quantity of nitrogen and does not vary with regard to the nonnitrogenous foodstuffs, after a few days one finds in the urine and fæces exactly as much nitrogen (and sulphur) as had been ingested in the food. This condition is called *nitrogenous equilibrium.* As an example the following experiment from Gruber may be given:

DAYS OF EXPERIMENT.	N-intake g.	N-output g.	Per cent dif.	S-intake g.	S-output g.
I. 1-5	90.00	89.81	– 0.21	......	......
6-12	131.60	132.75	+ 0.88	......	......
II. 1-2	35.80	36.16	+ 1.00	......	......
3-11	144.50	143.13	– 0.86	......	......
III. 1-7	154.81	153.02	– 0.51	......	......
8-17	213.72	213.26	– 0.21	12.77	12.79

D. EXAMPLE OF A METABOLISM EXPERIMENT

The following table after Atwater contains a summary of the ingesta and excreta in an experiment with mixed food. The experiment lasted four days, the subject being a man thirty-two years of age and of about 64 kg. body weight, who remained as quiet as possible throughout the experiment.

Ingesta, mean weight in g. per day

ARTICLES OF DIET.	Total weight.	Water.	Proteid.	Fat.	Carbohydrate.	N.	C.	H. in organic substance.
Meat	160	105.6	44.5	6.7	....	7.1	28.4	4.2
Butter	70	7.4	0.8	59.9	....	0.1	43.8	7.1
Skimmed milk	450	405.9	17.1	0.5	22.5	2.8	19 6	2.8
Maize, breakfast food	50	2.9	5.5	4.2	36.5	0.9	22.4	3.2
Sugar	64	....	....	...	64.0	...	26.9	4.2
Pepper cake	30	1.4	2.0	2.5	23.3	0.3	13.2	2.0
Water	1,500	1,500.0	....	...	....	...	....	...
Bread	310	129.3	24.5	8.7	143.5	3.9	84.7	12.7
Total	2,634	2,152.5	94.4	82.5	289.8	15.1	239.0	36.2

Excreta, mean weight in g. per day

Fæces	54.7	40.6	5.4	3.7	3.2	0.9	7.4	1.0
Urine	1,449.5	1,403.1	...	...	...	16.2	12.2	3.5
Respiration and skin.	......	962.8	...	...	...	....	207.3	...
Total	......	2,406.5	...	...	...	17.1	226.9	4.5
Balance	......	–254.0	...	...	...	– 2.0	+12.1	+31.7

If we consider the fæces as pure loss (cf. page 90), the body has disposed of (94.4 g. ingested — 5.4 g. excreted =) 89.0 g. proteid containing (16.2 — 2.0 =) 14.2 g. N, besides (82.5 – 3.7 =) 78.8 g. fat, and (289.8 – 3.2 =) 286.6 g. carbohydrates. In the urine 16.2 g. N were given off; but 2.0 g. of the N have come from the body itself—i. e., (6.25 × 2 =) 12.5 g. of the body's proteid has been lost. The total proteid metabolism, therefore, has been (89 g. + 12.5 =) 101.5 g. (or 16.2 × 6.25).

The ratio of N to C contained in proteid is 1 : 3.28. In the proteid destroyed by this man therefore there were 3.28 × 16.2 = 53.1 g. C. The total quantity of C eliminated in the respiration and in the urine was 219.5 g.; there remain 166.4 g. which must have been derived from nonnitrogenous food.

Of carbohydrates 286.6 g. (289.8 ingested – 3.2 excreted) were absorbed from the intestine, and this by calculation was found to have contained 124.7 g. C. Now we shall see later that carbohydrates burn in the body more easily than fat. We therefore deduct *first* the C belonging to carbohydrate. This leaves 41.7 g. C (166.4 – 124.7) which must have come from fat—i. e., since the fat used contained about seventy-six per cent C, 54.6 g. fat were burned in the body.

We conclude that the body has decomposed a mean quantity of 101.5 g. proteid, 54.6 g. fat and 286.6 g. carbohydrate per day. Comparison with the ingesta, having regard to the C resulting from proteid destroyed, shows that the body has lost 12.5 g. of its proteid but has stored up 24.2 g. fat, containing 12.2 + 6.5 g. C.

§ 2. POTENTIAL ENERGY OF THE FOODSTUFFS

The energy stored in a combustible substance is measured by the quantity of heat generated in its combustion, and is constant for every individual substance. The heat values of the substances most important for our present purpose, as determined by the calorimeter, are given in the following table. All data are for 1 g. of the substance and the heat values here, as elsewhere in this discussion, are expressed in large Calories (Cal.).

SUBSTANCE.	One g. of dry substance yields—	One g. of ash-free substance yields—	Author.
Proteid[1]	5.754 Cal.	5.778 Cal.	Rubner
Muscle (free of fat)	5.345 "	5.656 "	"
Animal fat	......	9.464-9.492 Cal.	Stohmann
Butter fat	......	9.231 Cal.	"
Grape sugar	......	3.743 "	"
Milk sugar	......	3.737 "	"
Cane sugar	......	3.955 "	"
Rice starch	......	4.183 "	"
Alcohol	......	7.080 "	Berthelot

When fat or carbohydrates are burned in the body, they are completely oxidized into carbon dioxide and water. If, therefore, the principle of conservation of energy is true for the body, the heat value of these substances as determined by the calorimeter must be their heat value in the body.

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[1] Meat extracted with water, alcohol, and ether.

Quite otherwise is it with proteid. The end products of its metabolism are not all completely oxidized, and hence contain not a little potential energy. To obtain the heat value of proteid for the body we must therefore deduct from its calorimetric heat value the heat value of the waste products resulting from its metabolism. This Rubner has done in the following way.

He fed a small dog with a proteid material whose calorific energy had been previously determined by combustion, and then determined the calorific energy of the corresponding urine and fæces. The former for 1 gram of proteid decomposed was 1.0945 Cal.; the latter, also for 1 g. of proteid, was 0.1854 Cal. Finally, he deducted 0.05 Cal. for the hydrolytic absorption on the part of the proteid while in the body and for the solution of urea. For 1 g. of dry proteid we would have therefore a physiological heat value of $5.754 - (1.0945 + 0.1854 + 0.05) = 4.424$ Cal.

In an analogous way the net physiological heat value of muscle deprived of its fat only was found to be 4.001 Cal., and that of the proteid of the body destroyed in fasting 3.842 Cal. For every gram of N found in the excreta after feeding the former we should estimate, therefore, 25.98 (6.25×4.001) Cal. and in fasting 24.94 (6.25×3.84) Cal.

Human urine yields on the average 8.0 Cal. for every gram of nitrogen contained. Human fæces, per 1 g. of N, yield all the way from 66 to 159 Cal., but per gram of organic substance the fairly constant value of 5.2–7.7 (mean 6.5) Cal. (Rubner, Atwater, Loewy).

In most metabolism experiments one has to deal not with pure lean meat, pure starch, or a definite kind of fat, but with a mixture of various fats, carbohydrates, etc. One must be content with the determination by direct analysis of the quantity of total proteid, total fat and total carbohydrate; for absolutely exact analysis of separate kinds of proteid, etc., would make all metabolism experiments impracticable. From such determinations as those above mentioned, Rubner calculated the mean dynamic value of the chief groups of the organic foodstuffs to be as follows:

1 g. proteid	4.1 Cal.
1 g. fat	9.3 "
1 g. carbohydrate	4.1 "

From the standpoint of the conservation of energy, it is to be assumed beforehand that these theoretical calorific values must be correct also for these substances when burned in the living body. In fact *we have direct experimental proofs of this*; and precisely because these proofs verify the assumption, they are of the greatest importance for the whole subject of physiology.

As long ago as 1883, Rubner showed by a long series of experiments, the details of which we cannot enter into here, that the different organic foodstuffs can replace one another in isodynamic quantities—i. e., in quantities which yield equal amounts of calorific energy. The foregoing assumption was sufficiently substantiated by these results alone. But Rubner carried his investigations still further (1894). By the use of the calorimeter he determined on dogs (direct calorimetry) the amount of heat lost, and at the same time estimated from the excreta the total metabolism (see page 92); then, from the calorific values of the foodstuffs, he calculated the amount of heat production (indirect calorimetry) in the body represented by this metabolism. The result was that in eight series of experiments covering altogether forty-six days the mean difference between the heat production as calculated from the metabolism and the heat loss determined by the calorimeter was only 0.3 per cent.

In some very careful experiments with men on a mixed diet Atwater has obtained similar results. In these experiments not only were the food and the total excreta analyzed, but the calorific values of the food, the urine and the fæces were determined directly; and at the same time the heat given off by the subject was measured by the calorimeter in which he was confined.

In the following table are summarized experiments taken at random from Atwater's papers, and in parallel columns are placed figures representing (1) the amount of heat production as calculated by him, and (2) the amount of heat loss determined directly. Besides, in order to test by these observations the heat values of the organic foodstuffs as given by Rubner, which are generally accepted as standard, we have calculated from Atwater's data the

MEAN PER DAY

		A	B	C	D	E	F
NUMBER OF EXPERIMENT.	Duration in days.	Heat production calculated by Atwater.	Heat loss determined directly.	Difference between A and B.	Mean of A and B.	Heat production calculated by the author.	Difference between D and E.
Rest.		Cal.	Cal.	Per cent.	Cal.	Cal.	Per cent.
5	4	2,482	2,379	− 4.1	2,430	2,501	+ 2.9
7	4	2.434	2.394	− 1.6	2,414	2,480	+ 2.7
8	4	2,361	2,287	− 3.2	2,324	2,359	+ 1.5
9	4	2,277	2.309	+ 1.4	2,293	2,292	− 0.04
10	4	2,268	2,283	+ 0.7	2,272	2,277	+ 0.2
13	3	2,112	2,151	+ 1.8	2.131	2,125	− 0.3
14	4	2,131	2.193	+ 2.9	2,162	2.127	− 1.6
23	3	2,216	2.176	− 1.8	2,196	2,154	− 1.9
24	3	2,238	2,272	+ 1.5	2.255	2,197	− 2.6
21	3	2,304	2,279	− 1.1	2,291	2,300	+ 0.4
25	3	2,242	2,244	+ 0.1	2,243	2,270	+ 1.2
26	3	2,043	2,085	+ 2.0	2.064	2,038	− 1.3
28	3	2,067	2,079	+ 0.6	2,073	2,071	− 0.1
Mean	45	2,244	2,241	− 0.1	2,243	2,245	+ 0.1
Work.							
6	4	3,829	3,726	− 2.7	3,777	3,819	+ 1.1
11	4	3,901	3,932	+ 0.8	3,916	3.936	+ 0.5
29	3	3,515	3,589	+ 2.1	3.552	3.549	− 0.1
31	3	3,439	3,420	− 0.6	3,430	3.434	+ 0.1
32	3	3,573	3,565	− 0.2	3,569	3.553	− 0.5
34	3	3,629	3,587	− 1.2	3,608	3,605	− 0.1
Mean	20	3,647	3,637	− 0.3	3,642	3,649	+ 0.2
Mean of all experiments	65	2,688	2,687	− 0.2	2,685	2,689	+ 0.2

amount of heat produced in each experiment by the destruction of proteid, fats and carbohydrates. These results are given in other columns.[1]

The greatest difference between A and B is 4.1 per cent, the least difference is 0.1 per cent. In the rest series the mean difference is 0.1 per cent, in the work series 0.3 per cent.

It is, therefore, conclusively demonstrated by Rubner's and by Atwater's experiments that the *foodstuffs generate the same quantity of heat when burned within the body as when burned outside the body.* From a comparison of column E with D, in the foregoing table, it follows also that the calorific estimation of metabolism by means of the standard heat values of the organic foodstuffs yields very satisfactory results in the light of the heat production as actually measured.

§ 3. METABOLISM IN FASTING

Quantitatively considered, metabolism takes the simplest form in the fasting condition, when the body is living exclusively at the expense of its own combustible materials. Hence it will be best to begin the discussion of the processes of metabolism with a presentation of that which takes place in fasting.

A. THE GENERAL CONDITION IN FASTING

It is commonly supposed that fasting is a very painful state. But this is not the case. Observations on starving animals as well as fasting experiments recently carried out on men show that no real pain is felt.

During the first day of fasting, especially at the usual meal times, there is a feeling of hunger, but it soon disappears; and it may even happen that when the individual is again permitted to eat, he has no real desire for food. Neither animals nor men have any great need for water during the fasting condition. Fasting dogs often do not drink when water is offered them, and fasting men give out much more water than they take in.

What is especially characteristic of the fasting condition is the progressive loss of strength. But even this is not always pronounced, as will be seen from the case of Succi observed by Luciani. Succi fasted for thirty days, and on the twelfth day he took a horseback ride lasting one hour and forty minutes; the same evening he walked around the room a great deal, ran an endurance race with three young students which lasted for eight minutes, and then went through a fencing exercise. On this day he took 19,900 steps. On the twenty-third day of his fast, he visited the theater in the evening, and there engaged in two bouts with swords, in which he showed endurance, strength and agility. On this day he took 7,000 steps.

The pulse frequency decreases during rest in the fasting state; but with very slight exercise it rises much higher than normal. The body-temperature (rectum) remains normal or falls only 0.1°–0.3° C., until within the last few days (third to ninth) before death by starvation, when it falls rapidly and suddenly. The body weight very gradually declines. The average daily loss in the first five to ten days of long fasting periods endured by men, has been found to be 1.0–1.5 per cent of the original weight.

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[1] Since the Calorie as used by Atwater is based upon water at a temperature of 20° C., and is therefore about 1 per cent lower than that usually employed (0° C.), we have used the following figures in this calculation: 1 g. proteid = 4.2 Cal., 1 g. fat = 9.4, 1 g. carbohydrate = 4.15.

During fasting a mass consisting of worn-out epithelial cells and residues of the digestive fluids accumulates in the intestine, which either during the fast or after it is broken is evacuated as fæces (cf. Chapter VII). From observations on fasting men, the daily quantity of fresh fæces is estimated at 9.5–22.0 g., of dry fæces at 2–3.8 g. They contain 0.113–0.316 g. of nitrogen, 0.44–1.35 g. of ether extract and 0.25–0.48 g. of ash. Microscopic examination of fæces reveals numerous fine, needle-shaped crystals of the fatty acids embedded within a finely granular, amorphous ground substance, but no true formed constituents.

B. CHARACTER OF THE METABOLISM IN FASTING

In fasting the total metabolism falls gradually from the first day onward. Estimated per kg. of body weight, however, the daily decline is only relatively small and remains for a long time at about the minimum reached at the beginning of the fasting period. As proof of this statement, we give here the results of a five-day fasting experiment on a man.

	Body weight ; kg.	Decomposed ; g. of—				Total metabolism, Cal.	Cal. Per kg. of body weight
		N.	Fat.	Carbohydrate.	Alcohol.		
Last food day	67.8	23.41	87	267	28	2,705	39.9
First fast day	67.0	12.17	206	...	..	2,220	33.2
Second fast day	65.7	12.85	192	...	..	2,102	32.0
Third fast day	64.9	13.61	181	...	..	2,024	31.2
Fourth fast day	64.0	13.69	178	...	..	1,992	31.1
Fifth fast day	63.1	11.47	181	...	..	1,970	31.2
First food day	64.0	25.44	64	250	22	2,437	38.1
Second food day	65.6	18.07	72	248	37	2,410	36.8

As is customary in fasting experiments, we have assumed that the total quantity of carbon from nonnitrogenous substances comes from fat. But the body contains at the beginning of the fast a certain quantity of glycogen, whose heat value calculated per g. of carbon is less than that of fat. This glycogen disappears for the most part during the first day of starvation and a part of the carbon reckoned as fat doubtless has its origin in this glycogen. Our figures for the total metabolism, during the first two fasting days at least, are, for this reason, too large; and hence it is possible that the body reaches its minimum metabolism on the first or second day of fasting.

To enter further into the processes of metabolism in fasting it will be necessary for us to discuss the decomposition of proteid and fat more fully. Nothing further can be said at present concerning the share of carbohydrates stored in the body in these decompositions, and in any case it must be regarded as unimportant in comparison with that of fat.

Experiments show that with well-nourished animals, having a plentiful deposit of fat in their bodies, the destruction of proteid gradually declines day by day until death; whereas with poorly nourished, lean animals after a preliminary fall there occurs a rise in the proteid metabolism, sometimes of considerable size.

This great diminution in the proteid metabolism in fasting, although occurring with various fluctuations, has been verified also for men. In the thirty-day fasting experiment on Succi the N-output on the tenth day was forty-nine per cent of the output at the beginning; on the twentieth day it was thirty-two per cent, and on the twenty-ninth day it was thirty per cent. In men also we meet with this peculiar relationship: the N-output in the urine increases from the third or fourth day, then falls off again (cf. table, page 96). The chief reason for this behavior probably is that on the first day the glycogen deposited in the body spares a part of the proteid from being destroyed; but since most of the glycogen is used up on this day, so that on the second day its protecting influence has ceased to exist, more proteid is then attacked. In this way the body must become impoverished in available proteid, consequently its destruction falls again and from now on the combustion in the body is maintained to a large extent by the fat, provided the body be not too poor in fat (Prausnitz).

From facts concerning metabolism after feeding, which will be summarized under § 4, we know that of all the foodstuffs ingested *proteid is the most easily decomposed*. Nevertheless in fasting the share of proteid in the total metabolism (calculated in calories) of animals previously well nourished is only seven to seventeen per cent. Inasmuch as this proteid comes from the tissues themselves, it follows that they are not by any means so easily decomposed as is the food proteid, or more correctly stated, they give up proteid from their own substance only in relatively small quantities.

The increase in the destruction of proteid which takes place in the later stages of fasting and which continues thence until shortly before death, is a very interesting phenomenon. Voit, who first observed the phenomenon, explained it by supposing that the fat had all been used up, hence the proteid metabolism was increased in order to keep up the energy requirements of the body. This conclusion was fully confirmed by the following experiment by Rubner. The N-output per day he found to be: first to third day, 1.67 g.; fourth to fifth day, 1.46 g.; sixth to eighth day, 3.21 g. The amount of fat burned proved to be: on the second day, 10.3 g.; fourth day, 10.3 g.; eighth day, 2.4 g.

When at the conclusion of the fast food is again supplied, the body shows a pronounced ability to make good its losses, and now lays on both proteid and fat in large quantities. In the five-day fasting experiment cited above the subject lost during the five days 399 g. proteid, 938 g. fat, 37 g. ash and 3,829 g. water. On the succeeding diet, which was a rich one, and of which 4,141 Cal. were absorbed daily, he destroyed a mean quantity for two days of only 2,424 Cal. daily, and thus recovered in these two days twenty per cent of the lost proteid, thirty-six per cent of the lost fat, seventy-one per cent of the lost water, and sixty-nine per cent of the lost ash.

C. LOSS OF SUBSTANCE FROM THE DIFFERENT ORGANS

In fasting the body *lives at the expense of its own substance*. On purely antecedent grounds it would be most natural to suppose that the o [illegible] in which the greatest amount of work is done would be destroyed to the greatest extent. But this is not true; on the contrary, these very organs seem to suffer the least loss of substance, while the loss is greatest from those organs upon which little or no demand is made in fasting.

If this conception be correct—and it must be admitted that direct observations are still very inadequate—it would follow that in fasting the organs do not do their work at the expense of their own substance. It seems that all the organs contribute to the support of the body; but those organs which are of primary importance for the maintenance of life, utilize the materials thus contributed by all, in the performance of their particular functions; that is to say, they *work at the expense of the less vital organs*: their own state of nutrition suffers less, and hence they decrease in weight relatively little.

This view receives support from certain experimental facts. The bones, for example, bear a part in the general levy made upon the organs. E. Voit fed pigeons with food which was sufficient in every other respect, but was very poor in calcium. The birds fared very well and were killed after some time. On section it became evident that those bones which were used in the movements of the animal were normal, while others such as the sternum and the skull were brittle and in places were even perforated. Since calcium was being lost from the body all the time, and none was being supplied in the food to replace it, the " resting " bones gave up their calcium to the " active " bones.

Probably a still more interesting example is furnished by Miescher's investigations on the Rhine salmon. This fish leaves the sea in the best condition of nourishment, but it remains in fresh water for six to nine months without eating anything. During this time it naturally becomes exceedingly thin and gaunt, and its muscles greatly diminished in size; but the reproductive organs become the more strongly developed. The substance of muscle has gone to make ova and sperm cells.

Sooner or later, however, there comes a time when the activity of the vital organs and of those most necessary for the generation of heat in the body, falls to the minimum. If animals be wrapped up in bedding they can be kept alive for a brief time longer. But respiration and the heart beat soon cease and the animal dies in a state of the most profound exhaustion.

§ 4. INFLUENCE OF FOOD ON THE METABOLISM

The most noteworthy thing about metabolism with food is the peculiar position which proteid occupies with reference to the other organic foodstuffs. If a dog be given a sufficient quantity of proteid with no fat or carbohydrate, under proper circumstances the body will remain in an equilibrium of substance, the ingesta and the excreta completely balancing each other. If, however, the dog receive carbohydrate and fat in plentiful quantities but no proteid, equilibrium never occurs. The body continually excretes nitrogenous waste products—which means that proteid is continually being destroyed—and after a time, which is somewhat longer than when no food at all is given, the animal finally dies of " proteid starvation."

Since we have no reason to suppose that there is any essential difference between the chemical processes involved in the final decomposition of the foodstuffs in the dog and in man, it is theoretically conceivable that a man also could be nourished exclusively with proteids. But the capabilities of the digestive organs must be considered. In man they are not able to digest and absorb proteid enough to maintain the body; hence man is always compelled to eat nonnitrogenous foodstuffs in addition to proteid.

A. INFLUENCE OF THE QUANTITY OF PROTEID IN THE FOOD ON PROTEID METABOLISM

This *exceptional position of proteid* prompts us to discuss the conditions of its metabolism first. Let us begin by inquiring how the quantity of proteid supplied to the body affects the proteid destruction therein. The following summary of a series of experiments by Bischoff and Voit may serve to give us our bearings. The animal received nothing but meat, which was carefully freed of fat, bones, cartilage, etc. The percentage of nitrogen in the meat is estimated at 3.4 per cent (corresponding to about twenty-one per cent of proteid).

EXPERIMENTS.	N ingested, g. per day.	N excreted, g. per day.	N-balance, g. per day.
No. 1	61.2	57.5	+ 3.7
" 2	51.0	51.4	− 0.4
" 3	40.8	41.9	− 1.1
" 4	30.6	37.1	− 6.5
" 5	20.4	23.1	− 2.7
" 6	10.2	15.4	− 5.2
" 7	6.0	12.5	− 6.5
" 8	0.0	7.7	− 7.7
" 9	61.2	58.4	+ 2.8
" 10	85.0	81.4	+ 3.6

From this and other similar series of experiments it follows without question: (1) that increasing the supply of proteid increases its destruction in the body; (2) that the entire supply of proteid, or, when it is large, almost the entire supply, is destroyed; and (3) that proteid is retained in the body (cf. numbers 1, 9, 10) only when fed in very large quantities.

EXPERIMENTS.	Food per day.		N excreted, g. per day.	N-balance, g. per day.
	g. N.	g. Fat.		
No. 1	5.1	250	7.9	− 2.8
" 2	8.5	250	9.2	− 0.7
" 3	15.3	250	11.7	+ 3.6
" 4	17.0	250	15.1	+ 1.9
" 5	25.5	250	22.4	+ 3.1
" 6	34.0	250	29.8	+ 4.2
" 7	42.5	250	39.2	+ 3.3
" 8	51.0	250	47.0	+ 4.0
		Starch.		
No. 1	23.8	150	26.3	− 2.5
" 2	20.4	150	23.1	− 2.7
" 3	14.6	200	18.8	− 4.2
" 4	8.8	250–350	13.4	− 5.6
" 5	5.1	350–430	10.7	− 5.6
" 6	0.0	450	5.7	− 5.7

The proteid metabolism behaves in essentially the same way when the diet contains a constant quantity of nonnitrogenous organic foodstuffs in addition to proteid. This may be seen from the preceding table.

Just as the body can destroy very different quantities of proteid, it can also be placed in nitrogenous equilibrium with very different quantities of this foodstuff (cf. first table on page 91).

The following experiments from Voit will give some idea of the time required to reach nitrogenous equilibrium:

I

Day.	N-intake, g. per day.	N-output, g. per day.	N-balance, g. per day.
No. 1	17.0	18.6	−1.6
" 2	51.0	41.6	+9.4
" 3	51.0	44.5	+6.5
" 4	51.0	47.3	+3.7
" 5	51.0	47.9	+3.1
" 6	51.0	49.0	+2.0
" 7	51.0	49.3	+1.7
" 8	51.0	51.0	0.0
II			
No. 1	51.0	51.0	0.0
" 2	34.0	39.2	−5.2
" 3	34.0	36.9	−2.9
" 4	34.0	37.0	−3.0
" 5	34.0	36.7	−2.7
" 6	34.0	34.9	−0.9

The two experiments were carried out on the same animal. Previous to the first the dog had received 17 g. of N (500 g. meat) daily. Equilibrium had not been established with this quantity, for on the last day of this period he lost 1.6 g. of N from the body. The supply of N (in meat) was then increased to 51 g.; immediately the N-metabolism rose, but perfect equilibrium was not reached until the seventh day, and during this time 26.4 g. N were retained in the body.

What became of this nitrogen? It might have been retained as dead proteid, as living protoplasm, or in the form of decomposition products. The last possibility has been rendered very improbable by various experiments of Voit. We shall return later to the question of whether the nitrogen is stored as proteid or as protoplasm.

The second experiment is just the reverse of the first. Here the animal had previously received 51 g. N (1,500 g. meat) and had been in nitrogenous equilibrium. The N-supply was then cut down to 34 g. The result was that on the very first day the N-excretion was less than before, and during the following days it sank lower and lower until on the fifth day it reached approximately the level of the amount supplied. During these five days the animal lost 14.8 g. N from his body.

Nitrogen excretion runs a similar course during the first few days of starvation. If the same animal be made to fast, in the one case after feeding a plentiful supply of meat, and in the other after feeding a scant supply, the excretion of N in the urine during the first few days behaves very differently: the greater the supply of proteid previous to starvation, the greater is the excretion of N during the first few days of starvation. It falls rapidly, however, and after about five days the amount of N eliminated is about the same whatever the composition of the food may have been previous to the experiment (Fig. 43).

Various circumstances favor the idea that this excess of nitrogen excreted from the body does not come from nitrogenous decomposition products left over from previous days, but that, in the transition from a N-rich to a N-poor diet or to fasting, a certain quantity of the proteid stored in the body undergoes decomposition until the organism has adapted itself to the diminished supply of proteid.

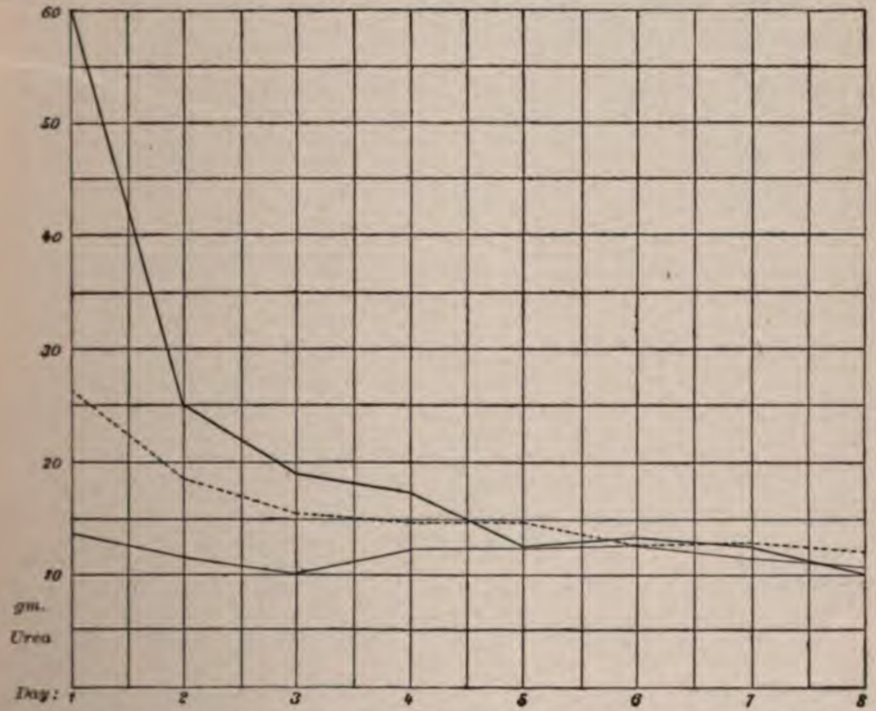

FIG. 43.—Three experiments on the elimination of urea by fasting dogs, after Voit. The food previous to the fasting period in the experiment —— consisted of 2,500 g. meat; in ------- 1,500 g. meat; and in —— only a little proteid.

The body places itself in nitrogenous equilibrium when the food contains both nitrogenous and nonnitrogenous substances, in exactly the same way as it does on an exclusively proteid diet.

The fact that proteid decomposition depends primarily upon the amount of proteid supplied is confirmed in a very interesting way by observations on the nitrogen excretion during the different hours of the twenty-four. The hourly excretion proves to be dependent to a very great extent upon the nitrogen absorption from the intestine. The curves in Fig. 44 will serve as an illustration. They represent the N-elimination in the urine in two-hour periods, from 8 A. M. until 12 P. M. The dotted line shows the elimination in fasting, the continuous line, on ordinary diet.

B. THE TOTAL METABOLISM AFTER INGESTION OF PROTEID

So far we have confined ourselves to the decomposition of proteid without inquiring how the *nonnitrogenous organic foodstuffs* behave at the same time. But in order to interpret correctly the phenomena just discussed we must consider also the metabolism of the latter—i. e., we must know the total metabolism.. As a basis for this discussion we may start with the famous experiments of Pettenkoffer and Voit on equilibrium, which are given in the following tables:

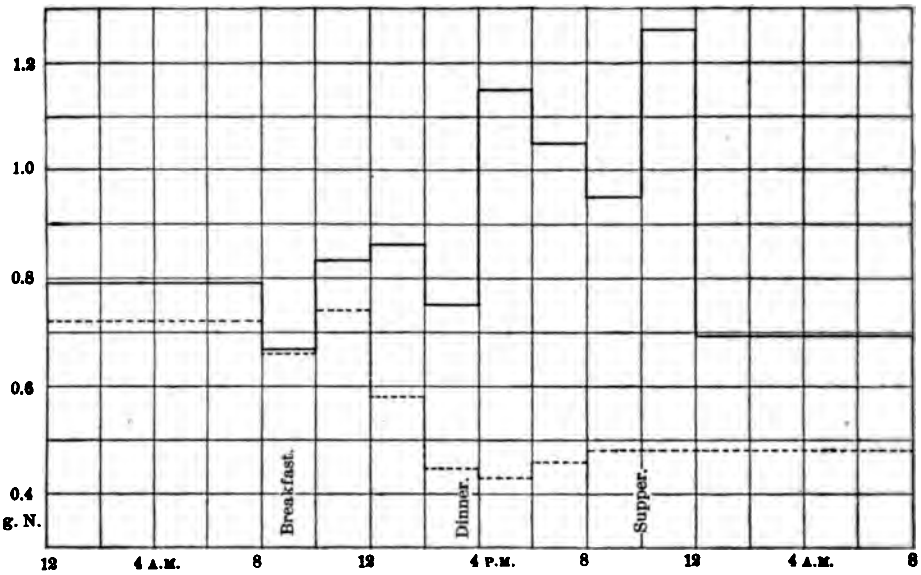

FIG. 44.—The elimination of N in the urine of man, determined every two hours, after Tengwall. ——— on ordinary diet; - - - - - - fasting.

In the first series of experiments meat only was fed. The nonnitrogenous metabolism is calculated from the carbon excreted (cf. page 90) and is estimated in terms of fat.

EXPERIMENTS.	N in food, g.	N excreted, g.	N-balance, g. per day.	Fat-balance, g. per day.	Total metabolism, Cal.
No. 1	....	5.6	−5.6	−98.0	1,067
" 2	17.0	20.4	−3.4	−61.0	1,106
" 3	34.0	36.7	−2.7	−43.0	1,360
" 4	51.0	51.0	.....	−24.0	1,552
" 5	61.0	59.7	+1.3	−36.0	1,893
" 6	68.0	69.5	−1.5	+ 8.0	1,741
" 7	85.0	85.4	−0.4	+ 4.0	2,181

In this and the following tables from Pettenkoffer and Voit, the carbon of proteid is calculated by the ratio, N : C = 1 : 3.28. [This ratio was first determined by Rubner in Voit's laboratory, but is generally attributed to Pflüger.—ED.]

We see that *as the amount of proteid fed increases the amount of fat burned decreases*, so that, when from 68 to 85 g. of N are supplied (in meat), a small amount of fat is stored in the body.

Estimation of the total metabolism in Cal. shows that as the amount of proteid in the food is increased, not only is the proteid decomposition increased but also the total decomposition, although the latter to a much less extent than the former. With 85 g. N (2,500 g. meat) in the food the total metabolism is about twice as great as in fasting or with 17 g. N (500 g. meat), whereas the proteid decomposition is fifteen times as great as in fasting and about four times what it is with 17 g. N in the food.

In his experiments on the metabolism of proteid in the body Voit thought he had found that the smallest quantity of proteid with which the body can place itself in N-equilibrium, even when carbohydrates or fats are administered freely, was higher than the quantity destroyed in starvation after the first few days of abstinence. Further investigations have shown, however, that in case the body receives enough nonnitrogenous foodstuffs to enable it to maintain a general equilibrium of substance, the quantity of proteid can be smaller than this.

From experiments by Hirschfeld, Kumagawa and Klemperer it appeared that N-equilibrium with small quantities of N in the food is only obtained when the total amount of food supplied is much in excess of the usual diet. Thus, while an adult man at rest maintains himself in N-equilibrium on about 100 g. proteid a day with a total energy supply of 32–35 Cal. per kg., in their experiments when the supply of proteid was cut down to 43.5 g., N-equilibrium only occurred when the total supply of energy was as much as 47.5 Cal. per kg.; and with 33 g. proteid only when the total supply reached 78.5 Cal. per kg.

Sivén has shown however that when the N-supply is not cut off suddenly, but is reduced gradually, no such excess of the total supply of energy is necessary. Under such circumstances N-equilibrium was obtained, in the case of a man doing a moderate amount of work, with 41.4 Cal. per kg. per day, although the diet contained only 28.3 g. nitrogenous substance. The quantity of actual proteid here was only 12.4 g. In other words, this man received only 0.08 g. total N per kg., of which only 0.03 g. was proteid N, and yet he maintained his N-equilibrium.

In the fasting experiment on Succi (cf. page 95) from the twenty-first to the twenty-fifth day, 0.09 g. N per kg. were excreted in the urine. In view of the long abstinence here, it is likely that this nitrogen came exclusively from proteid. This being true, it follows that the body can be brought into N-equilibrium with a supply of proteid which is considerably less than the amount destroyed in the later stages of starvation.

In experiments on dogs with food deficient in proteid but otherwise sufficient, I. Munk and Rosenheim observed from the sixth to the eighth week onward various severe disorders in the health, which finally led to the death of the animals some weeks later. According to this, a diet poor in nitrogen when taken continuously would be dangerous even if N-equilibrium were established. The experiments of Jägerroos stand squarely opposed to this view. They show that a dog can live much longer than eight weeks on such a food without exhibiting any disturbance to the health, provided he receive his proteid in the form of fresh raw meat. It appears, therefore, that in the earlier experiments it was not the deficiency of nitrogen itself, but the unsuitable character of the food which was the cause of sickness and death.

C. METABOLISM AFTER INGESTION OF FAT

If an animal be given as much fat as he uses from his own body in fasting, the latter is entirely replaced by the fat in the food. This will appear from the following observations on the dog (Voit):

A

EXPERIMENTS.	Food in g.	N excreted, g. per day.	Fat destroyed, g. per day.	Mean fat, g. per day.
No. 1	...	6.0	111	98
" 2	...	5.2	85	
" 3	100 fat.	5.4	93	97
" 4	100 fat.	4.5	100	

When the supply of fat is considerably greater than the amount of fat destroyed in starvation, its metabolism is increased.

B

EXPERIMENTS.	Food in g.	N excreted, g. per day.	Fat destroyed, g per day.	Mean fat, g. per day.
No. 1	...	11.6	96	103
" 2	...	5.7	108	
" 3	...	4.7	103	
" 4	350 fat.	7.7	167	...

At the same time the total metabolism becomes greater; in No. 1, table B, it amounts to 1,209 Cal., in No. 4, to 1,780 Cal. The increase is forty per cent. Quite similar results have been obtained in similar experiments by Rubner.

The following table contains a summary of experiments by Pettenkoffer and Voit on the total metabolism after feeding meat and fat:

EXPERIMENTS.	FOOD.		N excreted, g.	Fat destroyed, g.	Total metabolism, Cal.
	N. g.	Fat, g.			
No. 1	17.0	...	20.4	61	1,106
" 2	17.0	100	16.7	75	1,144
" 3	17.0	200	17.6	116	1,555
" 4	51.0	...	51.0	24	1,552
" 5	51.0	30	49.5	27	1,542
" 6	51.0	60	51.0	51	1,807
" 7	51.0	100	47.7	35	1,569
" 8	51.0	100	49.3	18	1,451
" 9	51.0	150	49.5	40	1,663

We have here two series of experiments on the same animal, the one with 17, the other with 51 g. N, and with varying quantities of fat in each case.

In the first the destruction of fat increases slightly with the amount of fat fed. In the second we see that the addition of 30–150 g. fat to 1,500 g. meat (51 g. N) increases neither the fat destruction nor the total metabolism. Metabolism, therefore, is not influenced by feeding fat to anything like the same extent that it is by feeding proteid.

D. METABOLISM AFTER INGESTION OF CARBOHYDRATES

In order to decide to what extent carbohydrates fed have participated in the total metabolism it is not sufficient to determine merely the N and C in the excreta; for we have in these data alone no means of telling how much C belonging to the nonnitrogenous substances came from carbohydrates and how much from fat. But if the O_2 absorbed in the same period be determined also, it is possible to decide whether the nonnitrogenous metabolism has been mainly from carbohydrates or mainly from fat.

When carbohydrates alone are burned the ratio between the *volumes* of carbon dioxide excreted and oxygen absorbed—i. e., the respiratory quotient $\left(\frac{CO_2}{O_2}\right)$—is just equal to 1; when fat alone is burned, it is only 0.71. The amount of CO_2-elimination and O_2-absorption corresponding to the proteid destroyed can be calculated without any difficulty from the N-excretion. But a certain quantity of carbon dioxide eliminated and of oxygen absorbed remains to be accounted for by the oxidation of fat or carbohydrate or both. Now if the respiratory quotient is high (near 1) we know that carbohydrates have participated to a great extent, but if it is low (near 0.75) we know that fat has entered largely into the metabolism.

So far only brief experiments performed by the use of the face mask have been made along this line. From these it may be gathered: that on a carbohydrate diet the respiratory quotient increases over that found in fasting; that the carbohydrates, therefore, are attacked immediately after their absorption from the intestine; and that in part at least they take the place of body fat in the general metabolism.

From these experimental facts it has been concluded further, that the carbohydrates fed are all destroyed before the body fat, and also before the fat in the food; and the results of all experiments in which carbohydrates are ingested by the body are calculated on this basis. This conclusion, however, is not fully warranted by the facts, and in opposition thereto it might be urged, among other things, that even in fasting the body protects its glycogen; and hence this carbohydrate at least is not all destroyed before the body fat.

The matter can only be settled positively by experiments covering a long period of time, in which either the amount of oxygen consumed or the amount of heat lost from the body shall be determined directly. Although unfortunately we have no experiments of this kind, still in the calorimetric studies of Atwater there are some very valuable results which permit us to take perfectly definite ground with regard to this question (cf. page 94). As mentioned before, the total transformation of energy in these experiments was both calculated indirectly from the heat of combustion of the food and excreta, and determined directly from calorimetric measurement of the heat given off by the subject of the experiment. In all the experiments carbohydrates were given in fairly large quantities and in the calculation of the heat values it was presumed, in conformity with the current view, that they were burned first. Now the experiments actually show a very close agreement between the calculated and the observed heat production. From which it follows that the theoretical presumption is a correct one, and that the total quantity of carbohydrates absorbed is burned before the body fat.

Especially instructive are two series of experiments in which both the total calories supplied (2,490 and 2,489 respectively) and the quantity of proteid were the same, but where the proportion of fat to carbohydrates was considerably different in the two. In the one experiment 94.8 g. fat + 247.2 g. carbohydrates were administered, in the other 40.3 g. fat + 375.2 g. carbohydrates. Direct calorimetric determination of the heat production yielded in the first 2,085 Cal., in the second 2,079 Cal., showing that the ratio of carbohydrates to fats within these limits at least is a matter of indifference to the organism.

Let us see now in which direction the addition of carbohydrates will influence the total metabolism.

Experiments of Pettenkoffer and Voit along this line gave the following results:

EXPERIMENTS.	N..	Food in g.		G. of N excreted.	Destroyed g. of		Total metabolism,[2] Cal.
		Fat.	Carb.		Fat.[1]	Carb.	
No. 1..........	....	....	...	7.3	103.0	...	1,164
" 2..........	....	16.9	379	7.2	– 56.3	379	1,208
" 3..........	17.0	....	...	20.4	61.0	..	1,106
" 4..........	17.0	10.2	167	19.3	– 19.9	167	998
" 5..........	17.0	4.6	182	18.3	– 10.9	182	1,117
" 6..........	17.0	10.3	167	18.0	– 14.0	167	1,020
" 7..........	51.0	....	...	51.0	24.0	...	1,552
" 8..........	51.0	17.5	172	50.2	– 38.1	172	1,649
" 9..........	61.2	....	...	59.7	36.0	...	1,893
" 10..........	61.2	26.5	379	50.0	– 112.9	379	1,782

From Experiments 1 and 2 it appears that the total metabolism after ingestion of carbohydrates (and a little fat) is not greater than it is in starvation, that carbohydrates therefore can completely replace the fat destroyed in starvation. From the series with 500 g. meat (17 g. N) no influence of the carbohydrates on the total metabolism is indicated. With 1,500 g. of meat addition of 172 g. carbohydrates produces only a slight increase (less than ten per cent), with 1,800 g. meat, 379 g. carbohydrates produce no increase at all.

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[1] A — sign means that fat has been stored in the body.

[2] 1 g. N = 26.0 (25.98) Cal., 1 g. fat = 9.46 Cal., 1 g. carbohydrate = 4.1 Cal.

E. SUMMARY AND DISCUSSION

It appears from the experimental facts brought together under divisions *Be* to *De*, that the ingestion of proteid always raises metabolism to a considerable extent, whereas ingestion of fat and carbohydrates either produces no increase, or at most only a slight one.

The experiments of Pettenkoffer and Voit, from which these conclusions are drawn, were not carried out in a continuous series, and it is possible that the result was due in part to the changed condition of the animal. The following series by Rubner is, therefore, more decisive, because the experiments came one immediately after the other:

Day.	N, g.	Ingesta.			Metabolism, Cal.	
		Fat, g.	Carb., g.	Cal.	Total.	Per kg.
2........	....	...	...	....	969	40.2
3........	56.8	...	...	1,513	1,072	44.8
4........	....	...	...	....	947	39.9
5........	....	167	...	1,536	963	40.9
6........	....	...	...	....	922	39.6
7........	....	...	411	1,446	982	42.3
8........	....	...	...	....	977	42.1

In fasting (days 2, 4, 6 and 8) the average metabolism was 40.4 Cal. per kg. of body-weight; on feeding 56.8 g. N it was 44.8 Cal. per kg.; with 167 g. fat, 40.9 Cal.; and with 411 g. carbohydrate, 42.3 Cal. The percentage increase over the fasting metabolism was therefore 11.9 for proteid, 1.2 for fat, and 4.2 for carbohydrate—although, as is evident from the table, the heat value of the food in all cases was almost exactly the same.

In another series on feeding 1,500 g. meat Rubner found an increase of 24.3 per cent over the fasting metabolism, and on feeding 153 g. lard or 456 g. carbohydrates, an increase of 5.1 per cent.

The results of Pettenkoffer and Voit are abundantly confirmed by these more recent experiments.

In explanation of the fact that increasing the supply of food produces, under certain circumstances, an increase in the metabolism, we might suppose either that the greater store of combustible material itself induces a more extensive combustion, or that the increase of total metabolism is due to the work of digestion or to muscular movements, etc. The matter can be definitely settled only by experiments on men where the voluntary movements can be controlled.

Both Magnus-Levy and Koraen have made such experiments and have shown that a clearly marked increase in the metabolism of the resting body makes its appearance only after ingestion of proteid. This increase, however, is scarcely to be ascribed to the work of digestion, but is rather the expression of a *special property* [what Rubner calls "specific dynamic action"—Ed.] of proteid to intensify the metabolism independently of muscular movements.

Nevertheless, it should not be asserted that the work of digestion causes no increase of combustion, for it is evident that the contractions of the gastric and intestinal walls as well as the secretion of the glands represent dissimilative processes, taking place with the liberation of kinetic energy.

The negative effect of fat or of carbohydrates on the total metabolism may be explained in one of two ways: either the work of digesting them is too small to produce a distinct rise, or the combustion in other parts of the body than the digestive organs is correspondingly reduced.

But this would apply only in case the bodily movements were suppressed as much as possible. We know from the subjective feeling of improved capacity for muscular work after eating and from an increased tonus of the muscles resulting from the mere ingestion of food, that the amount of metabolism may well be increased by the foods named, if voluntary movements continue. It is evident, however, that such an increase would be wholly independent of the kind of food, and would be only indirectly connected with the act of ingestion.

If the food be of such a quality or quantity as to make unusual demands upon the organs, the work of digestion may cause a considerable increase in the metabolism. Thus in one of Rubner's experiments in which 20–30 g. bones were fed, the metabolism rose ten per cent; and in an experiment of Magnus-Levy where 900–1,000 g. of bones were fed the absorption of oxygen increased twenty-four to thirty-three per cent during the first six hours. Likewise after administration of saline purgatives, Mering and Zuntz observed a distinct rise in the metabolism due to increased muscular activity of the intestine.

F. METABOLISM AFTER INGESTION OF ALBUMOSES, FATTY ACIDS, GELATIN, ALCOHOL, ETC.

Now that we have become acquainted with the metabolism after ingestion of each of the three principal kinds of organic foodstuffs, we shall consider briefly the food value of some substances closely related to them, which either are formed in the course of digestion, or occur more or less commonly in our ordinary articles of diet.

1. The digestion of proteid passes through a number of different stages (Chapter VII). It will be of interest here to inquire whether the substances representing these different stages are themselves all of equal value for the nourishment of the body.

If, with a constant quantity of fat and carbohydrate, an animal be given meat on one day, and on another the so-called protoalbumose formed in proteid digestion so that in both cases he receives the same quantity of nitrogen, the N-excretion and the N-retention exhibit no differences whatever in the two. This albumose, therefore, possesses the same food value as proteid (Blum). Heteroalbumose and peptone behave quite differently. They have the power to replace proteid to a certain extent, but it appears that they cannot maintain the body in N-equilibrium. The reason for this doubtless is that certain carbon nuclei of the proteid molecule which occur in protoalbumose are wanting in heteroalbumose and peptone. Investigations on the constitution of the different products of proteid digestion have shown in fact that the groups which yield tyrosin and indol do not occur in heteroalbumose. Since, apparently, the aromatic groups are not built up in the body, we can readily understand why heteroalbumose alone does not have the full food value of proteid. However, we are not justified in concluding from this that a part of the proteid ingested becomes of less value in the process of digestion, for it may well be supposed that all the digestive products taken together are of more service in metabolism than are single ones eaten alone.

2. On few physiological questions have opinions changed so much as on the food value of gelatin. It was once supposed that gelatin is the most important food constituent of meat, because it alone could be dissolved. Then the pendulum swung to the opposite extreme, and it was claimed that gelatin is of no food value whatever. Continued investigation has shown that both views were equally overdrawn.

Since gelatin, like proteid, is not completely oxidized in the body, its physiological heat value is less than that determined directly by the calorimeter. One gram of ash-free gelatin yields to the body 3.884 Cal.—i. e., 21.2 Cal. per 1 g. of N.

Voit, Oerum, and others have found that in its combustion in the body gelatin spares proteid to a considerable extent, acting in this way much more powerfully than equal quantities of fat or of carbohydrates (see page 120). Gelatin cannot completely replace proteid, partly at least because it lacks the tyrosin and indol groups. But by feeding gelatin the supply of proteid can be reduced considerably without disturbing N-equilibrium. Thus by feeding a quantity of proteid-free gelatin sufficient to cover one hundred and one per cent of the daily requirements of energy Krummacher found that the proteid destruction was reduced by about thirty-seven per cent of the amount destroyed in starvation.

[Murlin has recently shown that when the full calorific requirements of the body are made up with nonnitrogenous foods (of which a large percentage is carbohydrates), nitrogen equilibrium can be maintained in dogs and man, if two-thirds of the starvation requirements for nitrogen are supplied in the form of gelatin and the other one-third in the form of meat.

Kauffmann also has made a most beautiful experiment on himself. He established nitrogen equilibrium on a diet containing 42 Cal. per kilogram with casein as the source of proteid nitrogen. He then replaced the casein with a mixture of gelatin and certain amino acids, tyrosin, cystin, and tryptophan, which are lacking in the gelatin. The mixture contained exactly the same quantity of nitrogen as the casein and was distributed as follows: Gelatin, ninety-three per cent; tyrosin, four per cent; cystin, two per cent; and tryptophan, one per cent. Perfect equilibrium was maintained for a period of five days.—ED.]

Gelatin spares fat and carbohydrate as well. Thus a dog fed on 200 g. of gelatin lost only 15 g. proteid and 38 g. fat from his body per day, while on the eighth day of starvation the same dog lost 29 g. proteid and 102 g. of fat.

Gelatin and glutin-forming substances (which behave just like gelatin, Etzinger and Voit), play but a subordinate part, however, in the normal nutrition. They occur in the ordinary articles of diet in relatively small quantities, and to this extent have exactly the same importance as an equal quantity of proteid. When gelatin is fed in larger quantities to an animal, he soon refuses to eat. It must then be given forcibly by hand and soon causes indigestion. [Kauffmann complains of great languor and general indisposition for work during his gelatin experiment—effects which he ascribes to the lack of the extractive substances necessary to give the diet the proper flavor and to stimulate the nervous system.—ED.]

3. Fat is split up in digestion into fatty acids and glycerin (cf. Chapter VII). The former when fed alone have exactly the same effect on metabolism as a corresponding quantity of fat. I. Munk placed a dog in N-equilibrium with 800 g. meat and 70 g. fat. Then instead of the fat he gave the fatty acids derived from 70 g. of fat: the animal continued in N-equilibrium.

It has been shown that glycerin, which constitutes about nine per cent of fat and has a heat value per gram equal to about half that of fat, can be burned in the body and can spare both fat and proteid.

4. Cellulose, which forms so large a part of the vegetable foods, is acted upon by the digestive fluids of the lower animals (snail, Biedermann; carp, Knauthe); but in herbivorous mammals it is broken up only by the fermentative action of Bacteria, the end products being carbon dioxide, marsh gas, butyric acid, and acetic acid (Tappeiner).

It may be regarded as established that cellulose is dissolved to some extent also in the intestine of man. From twenty-five to sixty-three per cent of the cellulose of carrots, celery, cabbage and lettuce is decomposed in the intestine. Cooking appears to favor its solution. The cellulose in "whole-wheat" bread also is dissolved in considerable quantity (Hultgren and Landergren).

Nitrogen occurs in plants in a number of nonproteid compounds, which with the exception of asparagin (amino-succinic acid) appear to have no real food value. The case of asparagin is not without its practical interest, for this substance is a rather abundant constituent of leguminose seeds, oatmeal and potatoes.

5. It is perfectly certain that alcohol is burned in the body. Of the total amount absorbed from the stomach only about two per cent is eliminated from the body unchanged; the rest is oxidized to carbon dioxide and water (Atwater and Benedict).

If alcohol were destroyed in the body without protecting other substances from destruction, the CO_2-excretion ought of course to be correspondingly increased. But this is not the case. Experiments by Zuntz and Berdez and by Geppert show that a dose of alcohol, so long as it is not large enough to intoxicate, produces no appreciable increase in the consumption of oxygen, and only an insignificant increase, if any at all, in the excretion of carbon dioxide.—By means of experiments in which the total metabolism as well as the heat loss were determined directly, Atwater and Benedict were able to demonstrate also that alcohol can replace the nonnitrogenous foodstuffs to the full extent of its heat value.—Replacing a certain quantity of fat by an isodynamic quantity of alcohol produces at first a distinct increase in the destruction of proteid. If the experiments were interrupted at this time, the result naturally would indicate that alcohol does not save proteid, but rather intensifies its decomposition. If, however, the experiments be continued, the destruction of proteid falls again and comes back to the original level. The body therefore must become accustomed to alcohol, before the latter can exercise its proteid-sparing power (Neumann, Clopatt).

But alcohol cannot play any considerable part in the normal nutrition of man. The quantity which one unaccustomed to its use can drink without symptoms of intoxication is very small—only 16–25 g. With a heat value of 7 Cal. per g., this would amount to 112–175 Cal.—that is, estimating the requirements of metabolism at 2,500 Cal., 4.5–7 per cent of the total energy might be supplied in the form of alcohol. Only in very exceptional cases can alcohol be of any practical importance as a foodstuff. In diseases accompanied by reduced powers of digestion, it appears to be of great service as a direct food, quite independently of its effect upon the nervous system.

§ 5. INFLUENCE OF MUSCULAR WORK ON METABOLISM

It was apparent from Lavoisier's original experiments on the respiratory exchange that combustion is increased by muscular work, and investigations carried out since that time have established the fact beyond all doubt.

When Liebig, with much greater clearness than had been attained up to his time, had made out the chemical composition of foods and of the tissues of the dead body, he set himself the task of determining what foodstuffs are consumed in the work of the body and what significance in general the different groups of organic foodstuffs have for metabolism.

Since organisms are distinguished chemically by the fact that they contain proteid, he assumed that the activity of the body and especially of the muscles takes place at the expense of the living protoplasm, and that this in turn is built up from the proteid in the food. The nonnitrogenous substances, he said, are used in the formation of heat in the body by direct oxidation, and thus by taking possession of the oxygen they *protect proteid* from its harmful effects. On this basis the organic foodstuffs were classified as *tissue forming* or *plastic*, and *heat forming* or *respiratory*.

The second proposition of this hypothesis can be disposed of immediately. Experiment has shown definitely that decomposition of nonnitrogenous foodstuffs is not inaugurated by oxygen but by the activity of the tissues. The dependence of heat production upon the nervous system is evidence of this fact (cf. Chapter XIV).

If this view that bodily work takes place at the expense of the living substance of the muscles, were correct, one would expect that work would be accompanied by an increased output of nitrogen. But in the great majority of the experiments made to test this point *either no increase or only a very slight one* is found on working days.

The following experiments by Voit on the dog will serve as an illustration:

	N ingested, g. per day.	N excreted, g. per day.	
1. Dog............	..	5.6	resting
"	..	5.7	running
"	..	5.1	resting
2. Dog............	51	51.8	resting
"	51	55.3	running
"	51	51.8	resting
"	51	53.8	running
"	51	52.2	resting

The same result was obtained by Pettenkoffer and Voit in their experiments on man. The subject was required to turn a wheel with a crank—a kind of work to which he was accustomed—the wheel being so loaded as to demand about the same expenditure of energy as his customary work demanded. He worked nine hours of the twenty-four. Fasting and resting, he gave off 12.3–12.5 g. N; fasting and working, 11.7 g. On a moderate diet at rest, he eliminated 16.5–17.4 g. N and at work 17.0–17.4 g. N. Here likewise there is no increase in the daily excretion of nitrogen due to work.

Fick and Wislicenus made a very important experiment on themselves. They ascended the Faulhorn in Switzerland, a mountain which has an altitude of 1,956 meters above the lake at its base. Seventeen hours before the ascent they ate their last nitrogenous meal; the ascent itself lasted six hours, [illegible] hours later they ate the first nitrogenous food after the experiment. The urine was collected from the beginning of the ascent until seven hours after its conclusion, and was analyzed for nitrogen. Fick's urine contained 5.74 g. N and that of Wislicenus 5.55 g., representing a work equivalent, calculated from the heat value of the proteid burned, of 63,378 and 62,280 kilogram-meters respectively. Fick's weight was 66 kg. and Wislicenus's was 76 kg.; hence the amount of external work actually done in lifting their bodies 1,956 meters was 129,096 and 148,656 kg. m. respectively. The work done at the expense of proteid therefore could not have been more than one-half that expended merely in lifting their bodies, not taking into account the work of the heart, of the respiratory muscles and of the other muscles constantly in use in maintaining equilibrium.

But it might be argued that the increased excretion of nitrogen corresponding to the work of a given day would be eliminated from the body the following day. This idea, first expressed by Liebig, was tested by Argutinsky and Krummacher on themselves, and was reported by them to be correct. The force of their experiments is considerably diminished, however, by the fact that neither of the authors was in nitrogenous equilibrium during the resting days, and that their food was much too poor in absolute quantity of nutrient substances.

Moreover, Krummacher himself has shown elsewhere that when plenty of energy is supplied, the increased output of nitrogen on the day following work is quite insignificant. Thus a man engaged in hard labor received daily 89.3 g. proteid (=14.3 g. nitrogen), 175 g. fat, and 903 g. carbohydrate (=5,701 Cal.). During rest while on this diet, he excreted on the average 13.46 g. N in the urine and fæces. Then followed a workday on which he did 402,000 kg. m. of external work, and excreted 14.05 g. N. The output on the two following rest days was 13.70 and 13.47 g. N respectively. Only on the first of the two was there any increase over the elimination previous to the workday, and then it was only 0.24 g. N. This experiment also shows in a particularly beautiful way that muscular work is not done at the expense of proteid when a sufficient supply of nonnitrogenous food is given. The external work of the one day was equivalent to 945 Cal., whereas the total metabolism of proteid on the workday plus the excess on the day following (14.05 g. N + 0.24 g. N = 90 g. proteid) was equivalent to only 364 Cal.

But we are not to suppose that proteid cannot serve as the source of muscular energy. For in extreme cases when there is no fat and no carbohydrate at the disposal of the body, if muscular work is done, it can only be at the expense of proteid.

Pflüger fed a large dog for a long time on nothing but meat which contained as little fat and carbohydrate as possible. The dog was already very lean before the beginning of the experiment, so that there was no stored fat and glycogen to draw upon. From time to time he was compelled to do severe work varying in amount from 73,072 kg. m. to 109,608 kg. m., and since the fat and carbohydrate in the food were far from sufficient to produce this amount of energy, the work must have been done largely at the expense of the proteid.

It is perfectly easy to show that the *nonnitrogenous foodstuffs furnish energy* for muscular work. The excretion of carbon dioxide rises almost immediately as soon as work begins and has been known to increase from 27 to 131 g. per hour. There is no corresponding increase in the excretion of N, as we have seen, hence this excess of CO_2 must represent an increased oxidation of nonnitrogenous food.

In the experiments of Pettenkoffer and Voit on men, the daily amount of fat destroyed in fasting rose 171 g. as the result of work, and upon an ordinary diet it rose 101 g. The experiments of Atwater have yielded similar results. In one of his subjects the total metabolism during rest amounted to 2,357 Cal., of which 429 came from proteid, and 1,928 came from nonnitrogenous food. With severe muscular work the metabolism rose to the mean value of 5,119 Cal., of which 462 came from proteid, and 4,657 from nonnitrogenous food.

By parallel experiments, in which on the one hand chiefly fat, and on the other chiefly carbohydrates were fed, Zuntz has shown very definitely that the muscles can use one kind of nonnitrogenous food as well as the other. The same appears also from Atwater's experiments.

We can say, therefore, that the muscles are able to perform their work at the expense of *all three classes of organic foodstuffs,* that they prefer the nonnitrogenous substances, and, as it appears, they draw upon the carbohydrates first. Thus the one group or the other is utilized according to the kind of food eaten. The specifically carnivorous animals perform their muscular work at the expense of proteid and fat; the herbivorous animals, especially our domesticated farm animals, at the expense of carbohydrates, and in view of the large quantity of carbohydrates eaten by man the latter is probably true of the human body also.

It is of special importance for the physiology of general metabolism as well as for the physiology of the muscle itself, to determine how large a part of the increased transformation of energy accompanying muscular activity takes the form of external work.

For this purpose the respiratory exchange has been determined both during rest and while an accurately measured quantity of work was being performed. Subtraction of the carbon dioxide excretion and the oxygen absorption during rest, from the corresponding factors during work, shows an absolute increase which represents the known quantity of external work. In this way one can readily obtain the amount of metabolism which 1 kg. m. of work represents and these figures can be reduced to heat equivalents.

Such determinations have been made in Zuntz's laboratory in Berlin, and it has been found that the dog uses 0.007–0.0077 Cal. to do 1 kg. m. of external work and the horse 0.0069 Cal. at the same kind of work (walking uphill). And since theoretically 1 kg. m. = 0.00235 Cal., or 425 kg. m. = 1 Cal., we conclude that in these animals about one-third of the actual energy developed in muscular work appears as effective external work. In man the heat equivalent of 1 kg. m. of work with the lower extremities (mountain climbing) is about the same, namely 0.0072 Cal.; so that one-third of the total energy developed in our own muscles also is utilized as external work.

Even the slightest muscular movements influence the metabolism perceptibly, and if one wishes wholly to exclude this effect it is necessary voluntarily to suppress all muscular movements and tensions. Under such circumstances, that is, lying as quietly as possible, Johansson found the CO_2-excretion in himself to be about 20 g. per hour. Ordinarily while awake we never observe muscular rest so complete as this, and hence when Johansson merely lay resting in bed without special effort to suppress muscular movements, his CO_2-excretion rose to 25 g. per hour. In general we may say that the respiratory exchange in a man not doing any real physical labor, and yet not in absolute rest, is about forty per cent greater than in sleep.

§ 6. INFLUENCE OF THE SURROUNDING TEMPERATURE ON METABOLISM

The cold-blooded and warm-blooded animals react very differently toward changes in temperature. Whereas in the latter the respiratory exchange, which may be taken as a relative expression of the total metabolism, rises when the temperature falls, and falls when the temperature rises, in the former the respiratory exchange varies directly with the external temperature. The following experimental results, after H. Schultz, may be given as an example of the reaction of cold-blooded animals:

Temperature of the animal (frog). °C.	CO_2-output per kg. per hour.
1.0–1.6	0.008–0.015
6.4	0.067
14.5–15.4	0.069–0.085
25.0–25.3	0.150–0.171
32.5–33.5	0.550–0.670
34.0	0.639

It was first established by experiments from Pflüger's laboratory that when the external temperature declines the metabolism of warm-blooded animals increases over that characteristic of a medium temperature. *By increasing the heat production* the body protects itself against the heat loss occasioned by the cooling. Conversely, however, it is to be observed that a *rise of the body temperature* also produces an increase in metabolism; which shows that the energy of the oxidation processes in the warm-blooded also as well as in the cold-blooded animals increases with the temperature of the organs. There is here a fundamental agreement in the basal properties of living tissues in all animals. The increase of metabolism accompanying a decline in the external temperature is to be considered as a later acquirement on the part of warm-blooded animals—as something in fact which has been gradually evolved in the special interest of a constant temperature (Pflüger).

How exact this adjustment of metabolism to external temperature may be has been most beautifully shown by Rubner, as for example, in the following experiment on the dog:

Dog I.		Dog II.			
External temperature. °C.	Cal. per kg. per hour.	External temperature. °C.	Cal. per kg. per hour.	External temperature. °C.	Cal. per kg. per hour.
13.8	78.7	11.8	40.6	13.4	39.7
14.9	74.7	12.9	39.1	19.5	35.1
17.3	69.8	15.9	36.0	27.4	30.8
18.0	67.1	17.5	35.2		

The following experiment on a grown guinea pig fasting, is given as an example of the rise in metabolism appearing with a higher body temperature:

External temperature. °C.	Temperature of animal. °C.	CO_2, g. per kg. per hour.	External temperature. °C.	Temperature of animal. °C.	CO_2, g. per kg. per hour.
0.	37.0	2.9	30.3	37.7	1.3
11.1	37.2	2.2	34.9	38.2	1.3
20.8	37.4	1.8	40.0	39.5	1.5
25.7	37.0	1.5			

The influence of food on the metabolism at different external temperatures is a matter of great interest. The following experiment of feeding a small dog with different quantities of meat is one of the many published by Rubner on this subject.

External temperature. °C.	Calories per kg. and twenty-four hours.			
	Fasting.	100 g. Meat = 24 Cal. per kg.	200 g. Meat = 48 Cal. per kg.	320 g. Meat = 81 Cal. per kg.
7.0	86.4	....	77.7	87.9
15.0	63.0	....	....	86.6
20.0	55.5	55.9	57.9	76.3
25.0	54.2	55.5	64.9	....
30.0	56.2	55.6	63.4	83.0

From this and other experiments of the same purport we learn that with a sufficiently large supply of meat the metabolism becomes almost independent of the external temperature (experiment with 320 g. meat), while with a supply which is too low to furnish the calorific energy necessary even at a high temperature, the effect of the external temperature is felt to the full extent. This, in the judgment of the writer, shows that the ingestion of proteid beyond a certain limit increases the metabolism both at a high and at a low temperature. If the heat production obtained in this way alone is sufficient to cover the requirements of the body even at a low temperature, a fall in the temperature will have no power of itself to produce a further rise of metabolism. But if the rise due to proteid is not sufficient, a fall in the temperature will force the metabolism up, though to a less degree than when no proteid had been fed.

The *alterations of metabolism* in the service of heat regulation do not make their appearance, if the influence of the central nervous system on the muscles be terminated either by curare poisoning or by section of the spinal cord at a high level. This is shown by the following experiment of Velton on a curarized rabbit.

Temperature of the animal. °C.	Oxygen absorbed, cc. per kg. per hour.	CO_2 excreted, cc. per kg. per hour.
38.3	581	571
37.4	557	541
31.4	386	383
26.2	219	202
23.1	181	178

These facts naturally suggest that under normal circumstances the rise in metabolism here being considered is due to muscular activity called out by the central nervous system, and this is very generally assumed to be the case. But a question arises as to whether gross, plainly visible muscular movements necessarily occur.

In small animals, such as mice, the bodily movements become very active when the external temperature is greatly lowered. In dogs, on the other hand, Rubner never observed any movements which were directly occasioned by the heat or cold, although he emphasizes the statement that at the upper and lower extremes of temperature marked unrest was at times to be observed.

In the present writer's opinion, it is very difficult or probably impossible to solve the question of the part taken by the muscles in the heat regulation by experiments on animals, for there must always be a certain amount of muscular tension and the like which can scarcely be estimated with any accuracy, although the metabolism may be very considerably increased by them. Thus in experiments by Johansson, the CO_2-elimination in an ordinary resting condition, lying in bed, was twenty to thirty-one per cent more than when great care was taken to observe absolute muscular rest. Hence in order to exclude muscular movements altogether, it is obviously necessary to carry out the experiments on persons who are willing and able to enforce the desired state of relaxation of their own bodies.

From the experiments of Loewy it appears that within a period of one and one-quarter to one and one-half hours the respiratory exchange does not always increase, even though the temperature fall considerably. But whenever an increase did occur, if the experiment was being performed on an intelligent individual intrusted with the regulation of his own respiration, shivering or increased tone of the muscles was distinctly evident. By maintaining complete rest for one and one-half hours Johansson was unable to secure any evident influence of external temperature upon the excretion of carbon dioxide, although the body was naked and the temperature varied from 14° to 22° C. Under Rubner's direction, experiments continued from four to six hours gave, on the whole, similar results.

One is likely to conclude from these experimental facts that when muscular movements are voluntarily suppressed, the production of heat in man is for a time independent of the external temperature. But since, as Voit showed most clearly, the human body does undoubtedly react against the influence of a falling temperature by a more active production of heat, the conclusion we are to draw from the experiments just mentioned is rather that *visible muscular movements constitute the real cause of increased metabolism.*

§ 7. METABOLISM IN ANIMALS OF DIFFERENT SIZE

It is evident that, other things being equal, the total metabolism must vary with the mass of the body. But if, in animals of different size the metabolism be calculated according to the unit of weight, it proves to be *relatively greater in small animals* than in large ones.

This proposition may best be tested on fasting animals because the metabolism in them is constant, not being influenced by the kind and quantity of food. The following table, with the exception of experiment number one, is compiled from Rubner:

SPECIES.	Fast days.	Weight, kg.	Average of fast days per kg. of weight.		Calories.	
			N-excr.	Fat metab.	Per kg. weight.	Per sq. M. of surface.
No. 1. Man.......	3–5	64.0	0.20	2.81	31.2	995
" 2. Dog.......	6, 10	30.4	0.17	3.28	35.3	997
" 3. "	1–3	23.7	0.26	3.51	39.7	1,069
" 4. "	4, 8, 9	19.2	0.17	4.24	44.4	1,135
" 5. "	1, 3	17.7	0.31	3.94	45.0	1,040
" 6. "	2, 3	11.0	0.14	5.74	58.8	1,109
" 7. "	1, 2, 5	6.5	0.35	5.51	60.9	1,054
" 8. "	1, 3, 5	3.1	0.59	7.46	85.3	1,091
" 9. Rabbit.....	4, 5	2.6	0.58	4.00	52.2	615[1]
" 10. "	3–8	2.1	0.51	4.78	57.9	740
" 11. Guinea pig..	...	0.55	0.64	13.68	145.3	1,341

It is fairly evident that some variations between the different species of animals occur, probably because the covering of the body and some other bodily characters are not the same in all species. With this exception, however, the table shows a very uniform relationship, the cause of which will be apparent from the following considerations.

The smaller an animal is, the greater is its superficial area in proportion to its volume and weight. Suppose we have two balls, the one, A, 2 cm., the other, B, 4 cm. in diameter, the surface of A is then 12.56 sq. cm., that of B 50.24 sq. cr their volumes are 4.18 and 33.49 cc. respectively. In the smaller ball the ra of volume to surface is as 1:3, in the larger as 1:1.5. Now the animal b loses its heat very largely (about four-fifths) through the skin, and the qua tity of heat thus given off is evidently proportional to the skin surface. I order that the temperature may remain constant, the production of heat—i. the metabolism—must also be proportional to the skin surface. If, therefor a large and a small, warm-blooded animal with fur of the same thickness are to have the same bodily temperature in the same atmospheric temperature, the small animal must produce more heat in proportion to its weight than the large one—i. e., the metabolism per kilogram of weight must be greater in the former than in the latter (C. Bergmann).

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[1] [It has been shown that when the rabbit's ears are excluded th[illegible] ms exception.—Ed.]

In the experimental proof of this relationship which Rubner furnished later (above table numbers 2–8), he measured the superficial area of the body and calculated the metabolism per square meter of the surface. It proved to be the same for all the dogs regardless of size (last column of the table). The same relationship is demonstrable also for animals on food.

That the *growing organism* has a greater metabolism per kilogram of weight than has the adult, is evident from the mere difference in size. But experiment shows further that when calculated per square meter of surface,[1] the metabolism in younger individuals is higher than in older ones; in other words, the *metabolism is influenced by something peculiar to the young body,* which serves to keep it at a higher pitch.

The following table contains a number of observations by Magnus-Levy and Falk in support of this statement. They were made on individuals who had not eaten for some time and who were resting quietly, lying down.

MALES.			FEMALES.		
AGE. YEARS.	Weight kg.	g. CO_2-exc. per sq. M. surface per hour.	AGE. YEARS.	Weight kg.	g. CO_2-exc. per sq. M. surface per hour.
2½	11.5	17.7	....	....	....
6	14.5	17.4	7	15.3	15.7
6	18.4	15.5	6½	18.2	15.2
7	19.2	17.5	12	24.0	14.3
7	20.8	17.4	12	25.2	12.4
9	21.8	15.3	13	31.0	14.9
11	26.5	14.4	11	35.0	14.0
10	30.6	15.7	14	35.5	13.7
14	36.1	13.8	12	40.2	12.6
14	36.8	13.5	11	42.7	13.5
16	39.3	13.3	17–40	31.0–68.2	11.8
17	40.0	14.1			
14	43.0	14.0			
17	44.3	15.3			
16	57.5	12.4			
16	57.5	12.9			
22–56	43.2–88.0	11.2			

The few direct observations which we have on the *total metabolism* of growing children give the same result, as will be seen from the following summary:

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[1] The following formula devised by Meeh is used in calculating the superficial area of the body from its weight: $A=c\sqrt[3]{W^2}$, where W is the weight in grams and c is a constant empirically determined for each animal species. This constant varies somewhat with age, and for man it has a mean value of 12.3, for the dog, 11.2, for the rabbit, 12.9, for the rat, 9.1, and for the guinea pig, 8.9.

Age. Years.	Weight kg.	Total metabolism per kg.	Calories per sq. M. surface in 24 hours.	Author.
9½	23.2	63.0	1,499	Hellström.
9½	24.0	....	1,377	Rubner.
11	26.0	52.0	1,290	Rubner (not in N-equilibrium).
11	32.1	56.0	1,391	Sondén and Tigerstedt.
12	38.0	....	1,300	Rubner.
12	38.3	48.0	1,254	Sondén and Tigerstedt.
11	41.0	44.0	1,321	Rubner.
Adult	70.0	32.0	1,071	

The results of Camerer and others on the amount of food taken by children of different ages give exactly the same result. We give here only the figures obtained by Camerer.

Males.				Females.			
Age. Years.	Weight kg.	Calories per kg.	Calories per sq. M. of surface.	Age. Years.	Weight kg.	Calories per kg.	Calories per sq. M. of surface.
5– 6	18.0	77.0	1,680	2– 4	13.0	75.0	1,470
7–10	24.0	62.0	1,440	5– 7	17.0	69.0	1,460
11–14	34.0	47.0	1,250	8–10	22.0	59.0	1,390
15–16	53.0	40.0	1,220	11–14	32.0	52.0	1,330
17–18	59.0	38.0	1,200	15–18	41.0	33.0	930
Adult	70.0	32.0	1,071	21–14	45.0	40.0	1,150
				Adult	56.0	32.0	999

In *infancy*, as was to be expected, the metabolism per kilogram of weight proves to be much higher than in adult life; but calculated per unit of surface of the body it is decidedly less than in children somewhat older (cf. the following table). This is probably connected with the fact that the new-born child sleeps most of the time and the tonus of its muscles is but slightly developed.

Age. Weeks.	Weight kg.	Metabolism.		Calories per sq. M. surface.	Remarks.	Author.
		Total.	Per kg.			
9	5.1	352	69.0	1,006	Breast-fed.	Rubner and Heubner.
30	7.6	528	69.0	1,143	The same child fed on cow's milk.	" " "
30	7.6	569	75.0	1,233		
30	7.7	632	82.0	1,378		
2	3.2	258	81.0	1,000	The same child fed on cow's milk.	Camerer.
4	3.7	330	89.0	1,150		
7	4.4	440	100.0	1,370		
10	5.0	420	84.0	1,200		
14	5.6	440	79.0	1,170		
17	6.1	460	75.0	1,150		
20	6.6	470	71.0	1,120		

In *old age* the metabolism estimated by the square meter of surface is appreciably less than in middle life. While the CO_2-excretion in men between the ages of twenty-two and fifty-six was found to be 11.16 g. per square meter per hour, between the ages of seventy and seventy-seven years it was only 9.18 g.; for women between the ages of seventeen and forty it was found to be 11.75 g., between the ages of seventy-one and eighty-six, 9.79 g. (Magnus-Levy and Falk). The results of Ekholm on metabolism in the aged agree perfectly with these. This author found the mean of ten experiments on individuals between sixty-eight and eighty-one years of age to be 902 Cal. per square meter of body surface per day, while in resting men of middle age it amounts to 1,071 Cal.

We can say, therefore, that the *age of the individual* is one of the factors determining the intensity of metabolism, it being greater per square meter of body surface during the period of growth (with the exception of infancy) than in middle life, and greater in middle life than in old age.

§ 8. RETENTION OF PROTEID IN THE BODY

In our study of the decomposition of proteid in the body, supplied with meat alone, we found that but a few days elapse before the body places itself in N-equilibrium. The retention of proteid with such a diet continues therefore for only a short time and cannot reach any considerable amount. The greatest quantity of " flesh " which Voit was able to lay-on in dogs kept on a pure meat diet was 1,365 g. (= 46.5 g. N). On the average he was unable to bring about a deposit of more than 500 g. (= 17 g. N). With meat alone one may keep an animal in a uniform condition of proteid nutrition which has been attained previously in some other way, but once it is lost he *cannot restore this condition with an exclusively proteid diet,* nor bring about a " deposit of flesh."

From his experiments on an exclusive meat diet Voit drew the further conclusion that under circumstances otherwise the same, proteid is stored to a greater extent and for a longer time before N-equilibrium sets in, if the animal be already fat than if he be lean. In other words, the fat already deposited in the body saves the proteid fed from being destroyed and thereby permits a greater retention.

We have already seen that the N-output equals the N-intake even with a mixed diet composed of proteid and nonnitrogenous substances. But the *destruction of proteid* is *reduced* to a certain extent by the presence of these N-free substances; hence we might expect that a more extensive storage of proteid continuing for a longer time could be brought about by feeding nonnitrogenous substances with proteid.

Voit's many experiments with such combinations show this to be true. It is evident from these same experiments, however, that the saving of " flesh " is not much greater with a rich supply of meat than with a small supply. With 2,000 g. of meat and 250 g. of fat the daily sparing was 186 g.; with 1,000 g. meat and 300 g. fat it was 167 g., while with 1,800 g. meat and 250 g. fat it was 140 g., and with 1,500 g. meat and 150 g. fat, only 70 g. It is impossible to formulate any definite law from these experiments, but they appear to indicate that a large daily sparing of proteid depends not only upon the absolute quantity of meat, but is best attained when the supply of fat in proportion to the supply of meat is relatively large.

But we are concerned not so much with the conditions for a large daily deposit of proteid, as with those which insure a large aggregate deposit. It may well be that with a certain combination of meat and fat the daily deposit of proteid would be high, but would continue for only a few days; while with another combination the deposit per day would be less but would hold out longer, so that the total deposit would be greater in this case than in the first before N-equilibrium sets in.

It appears in fact from Voit's observations that it is not the greatest supply of proteid which brings about the greatest total deposit. With 1,800 g. of meat and 250 g. of fat N-equilibrium appeared in one case after seven days, and in this time there was a total retention of 854 g. of "flesh"; with the same animal on 500 g. meat and 250 g. fat, N-equilibrium did not appear within thirty-two days, but during this time not less than 1,794 g. "flesh" was laid on. With this combination the storage of proteid was very evenly distributed over the entire period: in the first twelve days the mean daily deposit was 71 g., in the following ten days 42 g., and in the last ten days 52 g.

In order to obtain the *greatest total deposit of proteid* in the body, just as for the largest daily deposit, it appears to be best, therefore, to give a relatively large quantity of fat in proportion to the quantity of meat. It is evident, of course, that the supply of proteid must not fall below a certain limit.

The carbohydrates bear the same relation to the retention of proteid as does fat, with the exception only that their proteid-sparing power is much greater than isodynamic quantities of fat.

This superiority of carbohydrates is shown in a very suggestive way by the experiments of Landergren. He gave an adult man an almost N-free diet, consisting (after deduction of the loss by fæces) of 1.6 g. proteid, 738 g. carbohydrate, and 17 g. alcohol, yielding altogether 45.2 Cal. per kilogram of body weight. On this diet the nitrogen excretion in the urine fell from 12.8 g. on the day before the experiment to 3.8 g. on the fourth day of the experiment. From the fifth day on the carbohydrates were almost entirely excluded, and instead an isodynamic quantity of fat was given (a net supply of 304 g. fat, 2.1 g. carbohydrate, and 30.4 g. alcohol, yielding altogether 43.7 Cal. per kilogram). On this diet the nitrogen excretion in the urine from the fifth to the seventh day rose as follows: 4.3, 8.9, 9.6 g.

In explanation of these facts it has been supposed that carbohydrates are in a less stable state of equilibrium, owing to their aldehyde or ketone groups, than fat is, and for this reason they are more readily decomposed and thus protect proteid to a greater extent. But this can scarcely be true, for as Landergren has shown, the carbohydrates exhibit their characteristic proteid-sparing effect even when they are fed with a considerable quantity of fat. Thus in an experiment with a net supply (i. e., deducting the loss by the fæces) of 6.5 g. proteid, 143 g. fat, and 308 g. carbohydrate, yielding altogether 45 Cal. per kilogram, the N-excretion in the urine on the fourth day was reduced to 3 g. The same thing appears from an experiment by Tallqvist, in which N-equilibrium was recovered just as easily with forty-four per cent of the nonnitrogenous energy supplied by carbohydrates as with eighty-three per cent. Therefore, in the presence of a certain minimum of carbohydrate, fat exercises just as great a N-protection as an isodynamic quantity of carbohydrate, whether N is being supplied in the food or not. The cause of this we shall discuss later.

We have no detailed experiments to show what conditions favor the greatest total deposit of proteid under the protecting influence of carbohydrates. But considering that the metabolism of proteid runs the same with carbohydrate feeding as with fat feeding, it is probable that there is an agreement in other respects also and that the storage of proteid is greatest when the proportion of carbohydrates to proteids in the food is high.

These results are of great practical importance, for they show that it is not best to feed a convalescent or a man in a poorly nourished general condition with proteid to the exclusion of other foods. Proteid cannot be deposited, and this means that the organs cannot be built up, on a diet composed only of proteid. Plenty of fats and carbohydrates are necessary as well as proteid.

It is generally supposed to be rather *difficult for the adult body to lay on proteid,* and this is borne out by the fact that N-equilibrium is very quickly established even with a very rich supply of proteid in the food. This behavior is really what one would expect. An excess of proteid would of necessity either raise its percentage in the fluids of the body (blood or lymph), or would be organized into the living protoplasm. The upper limit for the quantity of proteid in the former state is of course soon reached, and if still more proteid is to be retained, it can only be deposited as protoplasm. But, as v. Hoesslin has pointed out, the body seeks to maintain its normal mass of living substance within the narrowest limits possible; because a disproportionately large consumption is associated with the growth of cells, and with this large consumption there goes an increased functional capacity, just as a diminished capacity accompanies a falling off of living substance. The body maintains an average, even level of efficiency by keeping the mass of its functional parts approximately constant. The opposite of this, namely, an intimate dependence of the organism and of its functional state on the amount of protoplasm, or a rapid fluctuation in the mass of the body proteid would not be to the purpose—i. e., would be less advantageous than the existing arrangement. For this reason the body destroys most of the excess of proteid which it gets from the food.

Duration of Experiment in Days.	Calories per kg. body weight per day.	N-supply, mean per day, g.	N stored, mean per day, g.	N stored in per cent of N-supply.	Subject of Experiment.	Author.
15......	72.0	15.5	3.3	21	Self.	Krug.
27......	32.5–38.0	20.2–24.6	2.8	10–16	"	Dapper.
18......	70.0–90.0	17.2–24.2	3.8	15–26	Female patient.	Kaufmann and Mohr.
11......	67.0–96.0	15.0–17.3	5.7	34		

But, as appears in the table on the preceding page, with a sufficient excess of calorific energy a considerable storage of proteid can be accomplished even by the adult human body.

From this we see that while an excess of nourishment is of first importance for the retention of proteid, still other conditions are necessary. In adults, especially, muscular activity exerts a very great influence which cannot be explained solely by the greater supply of food which the working body demands. This is evident from the following experiment by Caspari.

A dog received a constant ration, containing 2,088–2,099 Cal. and 25.1 g. N per day. During rest the N-balance for three days was − 0.5, + 1.3, and + 1.2 g.; then followed a working period of four days with a daily N-balance of −1.4, 0.0, + 0.1, + 1.5 g. A period of rest inserted showed a N-balance of + 1.3 g.; whereupon the following five days at work gave + 2.5, + 3.7, + 2.9, + 3.5, + 3.5 g. At the same time the animal fell off in weight during the first working period from 33.0 to 32.6 kg., and in the second from 32.9 to 32.1 kg. In this case there was no excess of nourishment, and yet a considerable quantity of nitrogen was retained.

To study more closely the *conditions for the storage of proteid* in the growing body, and at the same time to exclude the influence of mere size, it is necessary to compare the metabolism of two individuals of the same size, one of which is grown and the other still growing. For this purpose Soxhlet has brought together the results obtained by him on a suckling calf 50 kg. in weight with those obtained by Henneberg on a grown sheep weighing 45.5 kg.

	In food per kg.		Grams N excreted per kg.	Grams N retained in body per kg.
	N, g.	C, g.		
Suckling calf	0.784	9.8	0.204	0.580
Sheep	0.212	5.6	0.167	0.045

From facts considered further back, we know that in the adult body the rule is for the quantity of nitrogen excreted to agree very closely with the quantity in the food. But, as the table shows, this is not true in the suckling calf. Hence, it follows that the *conditions for the combustion of proteid* in the growing body are much less favorable than in the adult body. And since this difference cannot all be due to the greater absolute quantity of food for the calf, we cannot choose but suppose that the cells of the growing organism possess a special ability to appropriate proteid from the fluids of the body, and to convert it into protoplasm. More than this we do not know at present.

From facts obtained on the dog, concerning N-metabolism with a low supply of N in the food, the view has often been expressed that in order *to protect a store of proteid* once obtained, as much proteid must be ingested as was necessary to acquire it, or at least that the supply of calories must be as great. But the experiments by Caspari mentioned above are opposed to this conclusion, and other observations tend in the same direction. It is evident from fasting experiments that the body offers great resistance to the dissolution of proteid once it has been organized into living protoplasm (cf. page 97); and the following experiment by Sivén shows that the body can maintain its status of proteid on a very small amount of proteid in the daily ration.

The subject was a man, thirty years of age, whose ordinary diet contained about 16 g. N daily (=100 g. proteid). By giving a correspondingly larger quantity of nonnitrogenous food, his proteid was gradually reduced to 6.3 g. N per day. The results are summarized briefly in the following table:

SERIES.	Number of days in experiment.	N-supply, g. per day.	Time before N-equil.	Total N-loss before N-equil.	Total N stored during series.
I...........	7	12.69	1 day.	0.53	9.73
II...........	8	10.40	1 "	0.34	6.04
III...........	6	8.71	At once.	....	4.39
IV...........	6	6.26	3 days.	2.09	−0.58

During this experiment the body not only did not lose proteid, but during the first three series it actually gained 20.16 g. N, and even in the fourth series lost but 0.58 g. That is to say, by proper adjustment of the diet the supply of proteid can be reduced to a very low level,[1] without entailing any loss of the body's own proteid.

Recently several authors, notably Loewi, have published observations according to which the final end products of proteolytic digestion not only can replace proteid[2] in the metabolism, but are able to bring about a N-retention in the body. If these observations should be confirmed in their entirety, the fact would be of the greatest significance for our conception of the metabolic processes. For the present we would not venture to express any definite opinion on the subject.

§ 9. STORAGE OF CARBOHYDRATES IN THE BODY

In 1848 Cl. Bernard and Barreswill reported that the liver differs from all the other organs in that it contains a large amount of sugar, whatever the character of the food. Some years later Bernard demonstrated that this sugar is produced by the liver from a substance difficultly soluble in water, and in 1857 he isolated this mother-substance as *glycogen*.

Glycogen is very widely distributed in organic nature and probably occurs in all animals. In the vertebrates it has been found in almost all organs where it has been sought, which must mean that glycogen is of great physiological importance in the body.

The amount of glycogen in the different organs varies considerably. It occurs most abundantly in the liver and the muscles, but in the latter it is to be observed that different muscles in the same animal may have a very different percentage of glycogen. Likewise, corresponding muscles on the two sides of the body do not have exactly the same percentages; hence it is not sufficient to analyze single muscles in order to obtain the amount of glycogen in the animal body.

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[1] For discussion of the optimum amount of proteid in the diet see page 142.

[2] Cf. also page 109.

In the following table are brought together some data on the percentage of glycogen in the new-born child, in a dog after a twenty-eight days' fast, and in the frog:

ORGAN.	New-born child. (Cramer.)	Fasting dog. (Calculated as sugar.) (Pflüger.)	Frog. (Athanasiu.)
	Per cent.	Per cent.	Per cent.
Liver	1.00–2.15	4.79	8.73
Muscle	0.87–1.85	0.16	1.00
Skin	0.05–0.07	0.03	....
Blood	....	0.01	....
Lungs	0.10–0.19	....	....
Brain	0.01–0.02	....	0.07
Ovaries	....	....	1.10

The total quantity of glycogen calculated as sugar in Pflüger's fasting dog was 52.5 g.—i. e., 1.5 g. per kilogram of body weight.

The *amount of glycogen* in the body is raised considerably by rich feeding. In a fattened goose, as much as 22.2 g. per kilogram of body weight has been observed.

From many analyses of the organs of hens and rabbits, Otto has found that the absolute quantity of glycogen in the liver is about half the total quantity in the body. The same appears from Pflüger's experiment on the fasting dog. When therefore Pavy found in the dog's liver alone a quantity of glycogen amounting to 7.82 g. per kilogram, it is to be supposed that the total quantity in the animal's body was about 15 g. per kilogram. Pflüger takes 11 g. as the average amount of glycogen per kilogram in the dog.

In man the glycogen in the liver is estimated at 150 g., and the total amount in the body at 300 g., which is only about 4 g. per kilogram. Possibly this estimate is too low.

Glycogen is laid down in the cells of the liver in large flakes (Fig. 45). It is deposited in the muscles partly between the fibrillæ and partly in them.

It is evident that glycogen must be formed in the liver because not only does it occur there in largest quantities, but when animals previously deprived of most of their glycogen by a fasting period are fed with carbohydrates, the liver is the first of all the organs to show a storage of glycogen. An independent formation of glycogen in other organs, and especially in muscles, is not thereby excluded, however, and in fact there are certain indications that glycogen is thus formed. For example: glycogen has been demonstrated in chick embryos before the rudiment of the liver appears, whereas the egg, before development, is said to contain no glycogen; the glycogen of the muscles of fowls presents certain differences from the liver glycogen; again paralyzed muscles are loaded with glycogen, etc. But this question probably ought not to be regarded as definitely settled.

In view of the great variations in the percentage of glycogen in the body, if one is to determine directly the influence of different foodstuffs on its storage, it is necessary first to deprive the animal, as far as possible, of all its glycogen. As appears from Pflüger's experiment on the dog cited above, a considerable quantity of glycogen may remain in the body even after prolonged fasting. Glycogen is far more completely removed from the body by severe muscular work; in fact under such circumstances it sometimes disappears almost completely, both from the liver and from muscles, in the course of a few hours. Naturally, the effect of muscular work is assisted by a previous fasting period.

There are a great number of different substances which have been claimed to bring about an increase in the percentage of glycogen in the liver. Among them are several which, at most, act only indirectly, either by stimulating the liver cells to produce glycogen or by diminishing its consumption. We shall pass over these substances and consider here only the true *glycogen formers.*

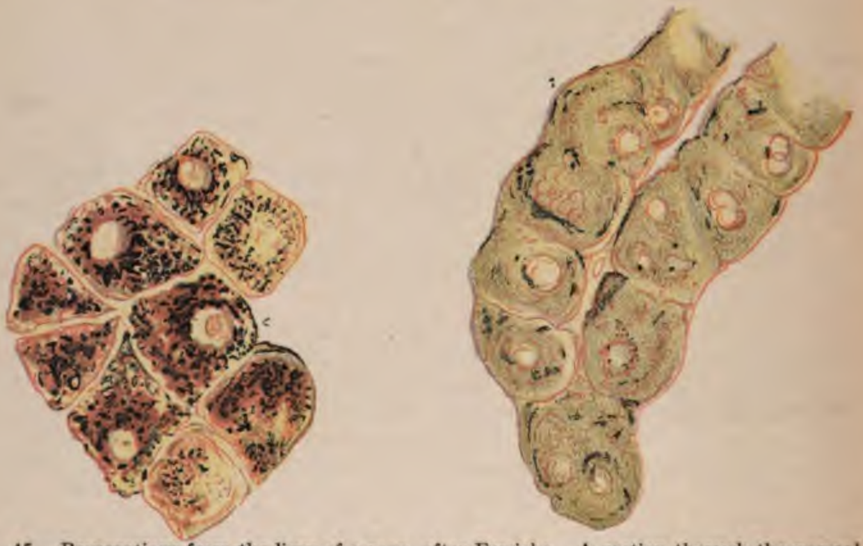

FIG. 45.—Preparations from the liver of a man, after Frerichs. A, section through the normal liver containing glycogen; B, section through the liver of a diabetic, almost free of glycogen. Both preparations treated with iodine.

There is no longer any doubt that *certain carbohydrates constitute an important source of glycogen*; proofs of this are present on every hand. For example, after feeding with cane-sugar, grape-sugar or starch, 14.7 per cent of glycogen has been found in the liver of hens, 10.5 per cent in that of the goose, and 16.9 per cent in the rabbit's liver.

It might be supposed that the carbohydrates had not contributed directly to this storage of glycogen, but that they only protect glycogen split off from proteid from being further oxidized. Otto has shown, however, that even if we assume that the greatest possible amount of glycogen has been formed from proteid, there always remains a considerable excess which could only have come from carbohydrates. Similarly Popièlski found that in dogs in which an Eck fistula had been made between the portal vein and inferior vena cava, but which were otherwise healthy, from twelve to twenty-four per cent of the sugar eaten was excreted in the urine. At least this quantity therefore is retained by the liver of normal animals (and is converted into glycogen).

The following carbohydrates at least can serve as a source of glycogen: dextrose, levulose, galactose, milk-sugar, cane-sugar, maltose, the last three after being inverted. In this connection it is noteworthy that the glycogen coming from levulose is also dextrorotatory. Levulose, therefore, is either changed first into dextrose, or it passes directly into a dextrorotatory glycogen; in either case the ketone group of levulose is transformed into an aldehyde group.

Many authors have found a *second source of glycogen* in proteids. In fact it has been observed that the quantity of glycogen in the liver increases after feeding meat extracted with boiling water, fibrin or chemically pure proteid substances. Pflüger on the other hand comes forward with the claim that the quantity of glycogen demonstrated in such experiments is not greater than the maximum which has been observed in fasting animals of the same species. Schöndorff found no increase of the glycogen in frogs after feeding them with casein.

The problem has been attacked also from another side. Under normal circumstances sugar appears in the urine only in mere traces; the total quantity of carbohydrate absorbed from the intestine is therefore either burned in the body, or is stored up after having been transformed into glycogen or into fat. It is only when the percentage of sugar in the blood, due to a rich supply of sugar in the food, exceeds a certain low limit (0.2–0.3 per cent), that a part of the sugar is eliminated through the kidneys (*alimentary glycosuria*). In this respect starch forms an exception to the rule for the carbohydrates, which is probably due to its relatively slow rate of digestion, a sudden flooding of the blood with sugar being thereby prevented. But in *diabetes mellitus* as well as after *complete extirpation of the pancreas*, or after *poisoning with phloridzin*, the body loses to a greater or less extent either its power to burn carbohydrates or its power to store them, and the urine under these circumstances always contains more or less sugar.

These facts have been made use of in attempting to determine whether or not sugar is formed from proteid. Thus, sugar appears in the urine in these diseased conditions after feeding proteid, and if it can be shown that this sugar actually comes from proteid, we should have proof that under some circumstances at least glycogen can be formed from proteid. For the sugar formed from proteid, as well as any other sugar, could, from what we have seen, be changed into glycogen.

It is a matter of great moment in these experiments to decide whether more sugar appears in the urine than can be accounted for by the glycogen already deposited in the body at the beginning of the experiment. Pflüger, who recently has subjected the observations on this subject to a searching criticism, takes the view that no proof has thus far been given for the formation of sugar from proteids. It appears, however, that this is going somewhat too far; for in many of the experiments, to explain the quantity of sugar appearing in the urine as derived from the body glycogen, it would be necessary to suppose that the animal at the beginning of the experiment had had its maximum percentage of glycogen; but this can scarcely have been the case in all the experiments.

[For example, Lusk and his co-workers have shown that producing phloridzin diabetes in fasting dogs may cause the proteid metabolism to rise 333 to 560 per cent. They have also shown that in these diabetic dogs, whether fasting, or fed on meat alone or on fat alone, no more fat is burned than in the same dog when he is normal and fasting. Thus, in one experiment a dog weighing 11 kg. burned on the second fasting day 20.19 g. proteid and 55.87 g. fat with a total of 606.81 Cal. Made diabetic, he lost on the fifth day 39.4 g. of dextrose in the urine. He burned on this day 67.38 g. proteid and 51.15 g. fat, a total of 605.77 Cal. The calories lost in the urinary sugar, therefore, are very exactly compensated for in the increased proteid metabolism. Since this dog had received only 115 g. of fat as food in the seven days, it is of course impossible that the great amount of sugar in the urine should have come from glycogen stored in the body (cf. also page 125). It must have come largely from proteid.—Ed.]

Recently the question of a final *conversion of fat into glycogen* has been actively discussed. As proof of this cases of diabetes occurring naturally or produced artificially have been cited, in which on a carbohydrate-free diet the quantity of sugar in the urine was too large to be accounted for by the proteid destroyed.

The first question to be asked in this connection is, how much sugar can proteid yield? In a number of experiments on dogs with pancreatic diabetes, Minkowski found the ratio of N to dextrose in the urine to be 1:2.8; in phloridzin diabetes, as v. Mering has shown, the ratio may be 1:5.[1] Remembering that for every 1 g. N in the human urine, on the average 0.72 g. C are eliminated by the same channel, and that proteid contains 3.28 g. C for every gram of N, the carbon remaining in the body which might go to form sugar would amount to 2.56 g. (3.28 − 0.72) for each gram of N ingested. Since dextrose is forty per cent carbon, 2.56 g. C would correspond to 6.49 g. dextrose and hence the utmost yield from proteid alone would be 6.4 g. dextrose for each gram of N.

In order to prove a formation of glycogen from fat it is necessary therefore that the proportion of dextrose to N in the urine should be greater than 6.4 to 1. [Now Lusk has shown that in phloridzin diabetes in dogs and in the most acute form of diabetes mellitus the ratio is fairly constant at 3.65 to 1; and nobody has ever positively observed a ratio so high as 6.4 to 1.—Ed.] For the present then we must say that *fat is not to be reckoned among the sources of glycogen* or sugar in the body. On the other hand it is fairly certain that glycerin is a mother-substance of glycogen.

Proceeding on the assumption that fat is not a producer of glycogen, Landergren has endeavored to explain the ability of carbohydrates, mentioned at page 121, to spare proteid to a greater extent than does fat. In his opinion the body has a specific need for carbohydrates. If they are not supplied in the food, they must be formed from proteid; hence the increase of proteid destruction when carbohydrates are excluded from the diet. Since in such experiments on man the N-excretion rose some 5 g. per day, the daily requirement of carbohydrates would amount to about 32 g. ($5 \times 6.25 = 31.25$; proteid Cal. = carbohydrate Cal.).

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[1] [In the experiments of Lusk and others a ratio as high as this is only obtained immediately after the injection of phloridzin, when there is a preliminary sweeping out of sugar.—Ed.]

§ 10. STORAGE OF FAT IN THE BODY

Voit laid special stress upon proteid as the most important source of the fat which is stored in the body. Using the ratio of N:C in proteid as found by Voit and Pettenkoffer, their experiments on the state of equilibrium actually show that a considerable portion of the C ingested in the form of proteid was retained. Since the formation of glycogen was never very large, Voit and Pettenkoffer were fully justified in concluding that some of the C was retained as fat.

But the percentage of C in proteid is not so high as Voit and Pettenkoffer supposed. Calculating their results on the basis of 1:3.28, the ratio of N:C now generally accepted, a very different conclusion is reached. Pflüger has shown that instead of 57.8–58.5 g. of fat, which Voit and Pettenkoffer estimated as the amount stored in the dog as the result of feeding 2,000 g. of meat per day, the newer ratio allows only 11.8–13.6 g., and that with 1,500 g. of meat practically no fat could have been stored. We are compelled, therefore, to conclude that these experiments contain no proof of a transformation of proteid into fat.

Later, however, Cremer obtained in the cat a retention of C from excessive meat feeding which he regarded as a safe indication of the production of fat from proteid. The cat excreted 11.2 g. of N per day and 31.2 g. C per day. But calculating the C from the N on the basis of the ratio of 1:3.2 would give 35.7 g. C as the amount ingested. Since only 31.2 g. of this was eliminated in the excreta, 4.5 g. of C per day must have been retained, and in seven days this would amount to 31.5 g. According to Cremer's subsequent analysis the animal's body contained not more than 40 g. of glycogen with 18 g. C. The remainder of the 31.5 g. of C, namely 13.5 g., must therefore have been laid on as fat. Unfortunately this experiment is quite too short and stands too much alone to be accepted as a positive demonstration of the point. (Gruber accomplished a retention of 81.9 g. C in a similar experiment on a dog, but the amount of glycogen was not determined.)

The other ground on which Voit based his idea that proteid is an important source of fat, was the degeneration of proteid under some circumstances into fat, and the great production of fat in the larvæ of blowflies living exclusively on meat. As regards the former, we now know that, at least in the case of the phosphorus poisoning of the frog (Athanasiu), the supposed fatty degeneration is in fact an infiltration of fat transported from the fatty deposits of the body and deposited in the cells, instead of a formation *in situ* by the destruction of proteid. Whether all forms of fatty degeneration are to be explained in the same way, has not yet been settled. Lindemann has found that the fat of the degenerated cardiac tissue is different in some essential respects from the fat deposited elsewhere in the body, as about the kidneys and under the skin. This fact, however, does not constitute strict proof against an eventual transportation of fat, for it is easily conceivable that the fat might undergo some change in the process of its liberation from the depository whence it came.

Pflüger explains the occurrence of fat in the larvæ of blowflies which lived on blood, as observed by Hofmann, by supposing that the fat was formed from the blood under the influence of Bacteria, and was merely absorbed as such by the larvæ. Moreover, as O. Franck has shown, the method of determining the fat, which was employed by Hofmann, does not permit of any positive conclusion from his experiment.

When we examine these observations critically, we must conclude with Pflüger that no single experiment has yet been given which proves beyond question that fat is formed from proteid. Since, however, most of the proteids contain a carbohydrate group and the body in all probability can form glycogen at the expense of proteid, and since carbohydrates are unquestionably a source of fat, the possibility of a final production of fat from proteid cannot be excluded entirely; although to judge from results thus far obtained, such a roundabout production is not large and never takes place except with a very rich supply of proteid. In man a transformation of proteid into fat is scarcely to be admitted at all, for he has the power to digest and absorb only a relatively small quantity of proteid.

On the other hand, we have any number of experiments which show that fat can be formed in the body *from nonnitrogenous substances.*

That fat given in the food can be directly stored in the body, follows from the experiments of Pettenkoffer and Voit cited on page 104, and is shown with particular clearness by the following experiment of I. Munk.

Munk let a dog starve for thirty-three days, during which time most of the fat was of course lost from his body. He then gave the dog 300 g. meat and 160 g. rape-seed oil daily for seventeen days, and killed him at the end of that time. On dissection a very large deposit of fat was found, which could not possibly have been derived from the meat fed. This in itself showed that the fat of the oil had been stored; but in addition to this erucic acid, which is a constituent of rape-seed oil but does not occur in dog fat, could be demonstrated in the fat laid down from the food.

Moreover, soaps and free fatty acids of the food can, after synthesis into neutral fat, be directly stored in the body. This Radziejewski and Munk have shown in the same way as in the experiment just mentioned, by feeding a soap of rape-seed oil and the fatty acids set free from mutton fat, respectively.

Whether or not *fat can be formed from carbohydrates* in the body, is a question which has been discussed for a long time. Since the latter spare fat from being metabolized, great importance has always attached to them in the laying on of fat, and weighty reasons were found for such a transformation in the case of herbivorous animals and especially of swine and cattle, which are fattened for the market very largely on carbohydrates. Thereupon, the discussion turned to carnivorous animals and man; and it has now been completely demonstrated by I. Munk and Rubner in experiments which we cannot go into here, that the transformation takes place in these also.

We see, therefore, that fattening always occurs if the supply of nonnitrogenous substances is greater than the needs of the body. Under such circumstances the body can store almost any quantity of fat. Underneath the skin, around the internal organs, in short everywhere in the body, fat can be accumulated.

§ 11. THE INORGANIC FOODSTUFFS

A. GENERAL

If an animal be fed proteid, fat and carbohydrates sufficient in quantity, but deprived as far as possible of mineral constituents, very evident disorders in the health of the animal soon make their appearance. Such food, poor in salts, will not be eaten voluntarily, and even though the animal may receive plenty of organic foodstuffs, and though he may absorb them for a long time in perfectly normal fashion, he becomes continually weaker and gaunter. Within two weeks symptoms of general weakness come on, the gait is sluggish and staggering, the muscles tremble, and the animal becomes exceedingly irritable in disposition. If the experiment be carried still further, convulsions ensue and finally death.

If, late in the course of events, the animal's ordinary diet be restored, at first he shows no desire to eat. The appetite however increases gradually, and finally becomes ravenous. The symptoms of weakness, trembling of the muscles, etc., pass away but slowly, and traces of them are to be observed for a month or more after the salts are restored to the diet.

It is perfectly certain therefore that the *mineral constituents* of the food are *just as important* as are the organic foodstuffs. In fact, it appears from researches by Forster, that the body can endure absolute abstinence better than it can endure deprivation of salts.

In order to understand the reason for this great importance of the mineral substances, it is necessary to know the effect of deprivation on the secretions and excretions of the body. We saw above that digestion goes on normally for a relatively long time; later, however (after three and one-half to four and one-half weeks), digestive disorders are exhibited. The animal vomits his food; or it may remain in the stomach for hours without being digested. In any case the vomited contents always contain a fairly large quantity of chlorine.

Forster has shown that the excretion of P_2O_5 never ceases entirely, it only becomes less than with the usual food; and, moreover, it decreases in proportion to the quantity of ash-free food ingested. The same is true of NaCl: during the first days of deprivation a relatively large quantity is excreted; later it falls off considerably so that finally in 200 cc. of urine only indeterminably small traces could be demonstrated. During the last days, when the animal was drawing heavily upon his own body for organic substances, larger quantities of NaCl were given off in the urine.

Forster considers himself justified by these experimental results in generalizing as follows: although the mineral constituents of the body are eliminated in smaller quantities when salts are no longer supplied, their excretion never ceases entirely. The quantity eliminated is least when organic foodstuffs are fed in abundance.

This is because mineral constituents for the most part form loose compounds with the combustible substances of the body, especially the proteids. When organic foodstuffs are not supplied in sufficient quantity so that the body must draw on its own store of these, the mineral constituents are set free, find their way into the fluids of the body, and are eliminated through the kidneys.

If an animal receive more salts in his food than he needs the excess is likewise eliminated in the excretions.

The importance of the individual elements has already been discussed on general lines at page 25. It remains for us to mention briefly the behavior of some of them in metabolism. It will be necessary to limit the discussion to phosphorus, calcium and magnesium. With regard to iron cf. Chapter X.

B. PHOSPHORUS

Phosphorus, like several other inorganic foodstuffs, is eliminated mainly in the fæces. In following the metabolism of proteids containing phosphorus we have therefore to consider both the urine and the fæces, whereas the metabolic products of proteids containing no phosphorus are almost all given off in the urine.

For a long time it was assumed that only the inorganic phosphorus compounds are absorbed from the intestine. This was based partly on results indicating that the excretion of phosphorus in the urine plainly rose after the addition of phosphates, and partly on the supposition that the phosphorus component of different proteids was indigestible. It has been shown, however: that pancreatic juice, acting for one to two hours, dissolves from one-half to one-third of the phosphorus in the nuclein of thymus (Popoff); that in the digestion of casein by gastric juice the greater part of the phosphorus passes into the soluble digestive products (Salkowski); and that under the action of pancreatic juice almost all of the phosphorus of casein is brought into solution (Sebelien).

It is not a difficult matter to show that the phosphorus from these substances is actually absorbed from the intestine. In some experiments on dogs Marcuse found that at least eighty-one to eighty-four per cent of the phosphorus of casein was absorbed; and in experiments on man Loewi observed an absorption of about seventy-nine per cent of phosphorus derived from nuclein.

But we cannot decide positively from these experiments whether the phosphorus is actually absorbed in *organic combination* or not. We know, indeed, that phosphorus is very easily split off from such substances by all sorts of agencies. In any case if it could be shown that phosphorus is stored in the body only after feeding with a proteid containing phosphorus in its molecule, we should then know that the body must depend upon such compounds as a source for this element. The experiments of Zadig seem in fact to prove that this is the case; but in a more recent series of experiments Leipziger was able to demonstrate a storage of phosphorus after feeding a P-free edestin and a phosphate. Hence there is as yet no proof that phosphorus may not be supplied as well in inorganic as in organic form. Experiments by Loewi have shown however that the ratio of N retained to P retained after excessive feeding with the nucleins agrees fairly well with the ratio of their percentages in the food, and indicates therefore that nucleins may be absorbed from the intestine, partly at least, in unchanged form.

In order to determine the absolute requirement of the human body in phosphorus it is necessary to measure directly the income and the output.

In human fæces the quantity of P varies, according to the character of the food and the P contained in it, from 0.25 g. to 3 g. and more per day. In the urine the limits for an adult are 0.4 g. and 2.8 g. When the phosphorus is drawn from the body itself, the quantity in the urine is less—only 0.4–0.7 g. per day. If after a period of deprivation plenty of phosphorus is supplied, the elimination in the urine is only about 0.9 g. The absolute need of the adult human body, therefore, would be 0.9 g. plus the amount in the fæces. But under ordinary circumstances in P-equilibrium, the quantity eliminated in the urine appears to be somewhat larger, and may be estimated at 1.5 g. Adding to this the average daily quantity in the fæces (0.75–1 g.), the total requirement of the adult body for P-equilibrium would be something more than 2 g.

C. CALCIUM AND MAGNESIUM

Both these elements are absorbed from the intestine in inorganic compounds. This we know from their appearance in the urine after the administration of calcium and magnesium salts.

An unlimited absorption of Ca and Mg is impossible because of the alkaline reaction of the blood, although it appears to be easier for Mg than for Ca. It is also very probable that Ca occurs in the blood only in the form of a proteid compound which is not precipitable by an alkaline reaction merely (Kühne). If, therefore, these elements occur in the diet in large quantities, the greater part is passed out unabsorbed in the fæces. Besides, Ca and Mg, like P, are excreted through the intestinal mucosa, proof of which is afforded by their occurrence even in starvation fæces. (In the case of Cetti 0.07 g. Ca and 0.006 g. Mg per day; in the case of Breithaupt 0.03 and 0.01 g. respectively per day.) With a diet extremely poor in mineral constituents generally, Renwall observed in the fæces an average of 0.16 g. Ca and 0.06 g. Mg per day.

When we compare the herbivora with the carnivorous animals we find considerable difference in the proportion of the calcium and magnesium excreted in the urine and the fæces. In the former, only about four to five per cent of the Ca and twenty-four to thirty-two per cent of the Mg appear in the urine, while in the latter, the urine contains as much as twenty-seven per cent of the total Ca excretion and sixty-five per cent of the total Mg excretion.

From the few observations thus far reported, we may judge that the excretion of Ca in the human fæces would amount to thirty-six to fifty-eight per cent of the total Ca excretion, and that of Mg sixty to seventy per cent of its total, the exact amount in each case depending on the power of the urine to dissolve the metal.

Very few attempts have been made to place the human body in an equilibrium of Ca and Mg, and for this reason it is scarcely possible to give definite figures as to the actual need for them. From the few facts at hand we may conjecture that an adult man would reach an equilibrium on a daily supply of 0.3–0.7 g. Ca, and of something more than 0.4 g. Mg.

§ 12. FLAVORS

A diet consisting of pure proteid, pure fat, pure carbohydrates, ash and water, each in sufficient quantity, would not be agreeable and would not be eaten except in case of extreme necessity. And yet we have in such a diet everything that one needs with a single exception—namely, something to give the food an agreeable taste and odor; in short, a *flavor* to make it palatable. We must not suppose that this aversion to the pure foodstuffs is due to the love of pleasurable sensations which characterizes man in the civilized state, for an animal will not voluntarily eat a perfectly tasteless food, even if it contains everything that he needs.

We may reckon among flavors not only the substances commonly understood by the word in its strictest sense, such as that which gives the characteristic taste to roast beef, or that developed in the baking of bread, the spices, extracts, etc., but also coffee, tea, alcoholic drinks, tobacco, etc.—in short, anything which adds to a meal an element of pleasure. In this sense we might include also the various extraneous means of making a meal enjoyable, like neat service, lively conversation, etc.

Some of the foodstuffs themselves serve at the same time as flavors—e. g., sugar and salt. The body requires NaCl; but in the quantities in which we ordinarily eat salt, it is really a flavor.

The *physiological importance of flavors* consists in the stimulus they afford for the secretion of the digestive fluids. Sight or smell or even the thought of an appetizing dish makes the mouth water—i. e., makes the salivary glands secrete profusely. As we shall see later under digestion, the same can be demonstrated for the gastric glands. If a meal or its accompaniments are not pleasant, these reflex effects are not forthcoming (cf. Chapter VII).

If one eats too much or too frequently of a dish once palatable, it becomes distasteful or even "turns against" him; and the more pronounced the taste of the dish, the more quickly will it become distasteful. On this account there are only a few articles of diet, such as bread, which we can eat every day or in large quantities. Herein lies the importance of variation in diet, even different modes of preparing the same articles being advantageous. For example, the people who live mainly on flour or meal of cereals do not eat these substances exclusively in the form of bread, but use them also in the preparation of dumplings, noodles, pancakes, etc.

§ 13. ON THE THEORY OF METABOLISM

In order to comprehend fully the processes of metabolism it is needful that we inquire to what extent, if any, the *organized substance of the body* is broken down in combustion.

When we consider how very much the destruction of proteid depends upon the amount ingested (page 99), how the N-excretion after meals is very closely connected with the absorption of proteid into the blood (page 101), and when we remember that the nonnitrogenous foodstuffs do not essentially alter the destruction of proteid (page 105), and that physical work with plenty of N-free foodstuffs supplied does not increase the proteid combustion (page 111), we are almost compelled to suppose with Voit that it is the proteid of the food and not the living protoplasm which first breaks down in metabolism.

Since the living protoplasm is derived from proteid, and upon its degradation after death again forms proteid, it is quite common in the physiology of nutrition to apply to it the name of tissue proteid, and to the dead proteid coming from food and found in the fluids of the body, the name "circulating proteid." In order to avoid misunderstanding we shall use here the terms: *living substance*, in whatever tissues it may occur, and *food proteid*—i. e., the proteid absorbed from food but not transformed into living substance.

The *food proteid* is distinguished in the first place by the ease with which it is destroyed by the organs of the body. No other organic foodstuff can compare with it in this respect. It is true that fat and carbohydrates, if supplied in sufficient quantity, can reduce the destruction of proteid to a certain extent, but in a general way this destruction bears about the same relation to the proteid ingestion whether the N-free foodstuffs be eaten or not.

The digested proteid passes into the blood as food proteid. If the quantity absorbed is not too small, and if at the same time plenty of N-free foodstuffs are present, a part of it may remain in the body undestroyed, but, as a rule, the greater part of it is destroyed within twenty-four hours.

In sharp contrast with this is the fact that the mass of living substance has but a very slight influence on the amount of proteid destroyed. We have seen (page 117) that there is no direct proportion between the weight of the body and the amount of proteid metabolism, and (page 124) that beyond a certain lower limit the body can maintain its proteid status on widely different quantities of proteid, provided only that the nonnitrogenous foodstuffs be present in sufficient quantity.

It follows, therefore, that the *living substance is not destroyed* either in the metabolism of proteid or in that of the nonnitrogenous foodstuffs, but on the whole is relatively stable.

The doctrine of Voit, given preference here, that the food proteid is destroyed first and the living substance only when the food proteid is not sufficient for the needs of the body, is still disputed by many authors of high rank, who advocate the view, first put forward by Liebig, but modified later by Pflüger and others. According to this view the living molecules of which the cells are composed are continually being destroyed and built up again in the life process; the cells as such do not break down, but their molecules are incessantly changing; the living molecule disintegrates much more easily than that of dead proteid, and the latter is destroyed only after it has been transformed into living molecules; of itself it is much more stable than the living substance.

It is indeed a matter of everyday experience that when an organ is taken out of the living body, it dies within a relatively short time, and on the other hand, that dead proteid in a dry condition can be preserved for any length of time unchanged. But we are not to conclude from such observations that in the living body, dead proteid is less destructible than living protoplasm. For an extirpated organ, by the very act of its removal from the body, is placed in altogether abnormal circumstances. In the living body the medium in which the cells and the tissues carry on their activities is the lymph. Wherever this fluid is wanting, or has not the proper temperature and the normal constitution, is not renewed often enough or is not provided with sufficient oxygen, protoplasm there represents a very destructible substance. But we are not justified by this alone in maintaining that the living substance behaves in the same way, when the lymph is perfectly normal. What we know is, that when the lymph is normal, the living substance carries on its functions; and there is no ground for the assumption that it is then less stable than the dead substances found in the fluid by which it is bathed.

If the living substance were always breaking down when it is active, what a tremendous work of synthesis would be required in order to keep it restored from the dead food proteid! And if this were true, how should we explain the extraordinary difficulty with which the adult body lays on proteid? If the food proteid had first to be organized in order to be used by the cells, the same would of necessity be true of the nonnitrogenous foodstuffs, of alcohol, etc.; before they could be destroyed they would have to become integral constituents of the living substance. We cannot get away from this consequence; but what direct proof have we for it?

How much simpler is the other view that the organized tissues do not themselves break down—their molecules not being destroyed—during activity, but are relatively stable substances which perform their duties at the expense of the combustible stuffs present in the lymph; that the tissues draw upon the lymph for whatever they require; that in all probability they take up these stuffs (proteid, fat, carbohydrate, etc.), into their own mass, not, however, organizing them into their own substance, but destroying them sooner or later, according to the intensity of their vital activities, as so much fuel.

In so regarding the living substance as relatively stable, we do not mean to say that, longer periods of time considered, it may not be destroyed and be restored again. Indeed, it will be found expressly stated under the appropriate sections, that certain organized structures, like the blood corpuscles, epidermal cells of the skin and its appendages, epithelia of the intestine, etc., are all the time breaking down and being lost, and it is more than probable that the other tissues exhibit the same phenomena.

There is another question, the satisfactory solution of which is of the greatest importance for this conception of metabolism, namely, Why is it that with sufficient nonnitrogenous foodstuffs to cover the calorific requirements of the body, it cannot entirely dispense with proteid in the food?

Of course this is partly due to the fact that the living substance is being destroyed to a certain extent, and needs proteid for its restitution. More than this, proteid is used up in the formation of the digestive fluids, in the secretion of milk, etc. Just how great is the quantity necessary to cover these absolute requirements of the body, cannot be stated at this time; but it is considerably less than the quantity which appears to be necessary to maintain the body in a satisfactory state of nutrition.

Voit answered the question before us by simply saying that the tissues have need of a certain amount of proteid for their own maintenance. But this answer is only another way of stating the facts to be explained. The following appears to throw some light on the question.

The lymph is the medium in which the cells and the tissues live. It contains proteid as one of its necessary constituents. But when proteid is present, it is destroyed by the tissues with the greatest avidity. In starvation the proteid of the lymph, therefore, is gradually used up, so that the latter would become unsuitable as a medium for the tissues, if they did not themselves give up some of their proteid to the lymph. This proteid is in its turn destroyed, and a new moiety from the tissues takes its place. Thus it goes on continually; and our question, why proteid is destroyed in the body not only in starvation but even when the supply of nonnitrogenous food is as great as possible, is to be answered through this continual need of a lymph with the same peculiar constituents all the time, and through the peculiar preference of the cells for proteid before all the other organic foodstuffs. Such an explanation does not require us to suppose that the tissues or the organized molecules themselves must break down with every manifestation of life. From the same point of view we can explain also the phenomena attending deprivation of salt (cf. page 131).

[On the basis of some very thorough studies of the composition of normal human urines following different diets, Folin has worked out a theory of proteid metabolism which has received such extensive notice as to deserve mention in this connection. Folin finds that in order to explain the changes in the composition of the urine with reference to nitrogen and sulphur, it is necessary to assume that the proteid metabolism is of two kinds. "One kind is extremely variable in quantity, the other tends to remain constant. The one yields chiefly urea and inorganic sulphates, no creatinin and probably no neutral sulphur. The other, the constant metabolism, is largely represented by creatinin and neutral sulphur and to a less extent by uric acid and ethereal sulphates."

The variable metabolism is conceived as consisting of a series of hydrolytic splittings of *food proteid* (cf. Chap. VII), begun in the intestinal wall and completed in the liver, which result in the elimination of the proteid nitrogen as urea. This is called *exogenous metabolism.* The constant metabolism represented by creatinin (and uric acid) is regarded as a true index of that destruction of *living substance* necessary to the continuation of life, and is therefore called *endogenous metabolism.* In Folin's view, only that amount of proteid necessary for the endogenous metabolism is really needed by the body. The greater part of the proteid in ordinary diets, i. e., that amount representing the exogenous metabolism, is not needed, or at least its nitrogen is not needed.

This theory agrees with Voit's theory as stated above in regarding the living substance as relatively stable, but differs from it in regarding the more ready dissolution of ingested food-proteid not as a matter of preference on the part of the cells, but as a specially developed means for removing the unnecessary nitrogen of the proteid ingested. The carbonaceous part of the proteid molecule, which alone is conceived as undergoing true oxidations similar to those which fats and carbohydrates undergo, is thereby rendered available.

The theory seems to explain the facts of proteid metabolism as stated by the author in this chapter quite as well as Voit's theory, and in addition seems to place a new physiological significance on the portal circulation.—ED.]

SECOND SECTION

NUTRITION OF MAN

If the diet contains in sufficient quantities and in the proper proportion all those substances which the body needs, it constitutes what Voit calls a "food." As applied to a healthy adult man, this ration is that quantity of foodstuffs which is necessary to keep the body in an equilibrium of substance. For growing children as well as for adults in a poor state of nutrition, the ration must be more plentiful so that a part of it can be retained in the body.

In this section we have to study the *nutritive requirements* of man and some of the circumstances affecting them. Naturally we cannot go into details here; important as they are, they belong to hygiene and dietetics, rather than to the physiology of nutrition.

The nutritive requirements of a man are represented by those quantities of the different foodstuffs which must be added to the body from the intestine every day. But inasmuch as we do not commonly eat pure foodstuffs, but meals prepared from various articles of food, the question may be raised, whether the foodstuffs contained in the different articles of food are utilized in the intestine to an equal extent. Experiment has shown that as a matter of fact the utilization of the foodstuffs in different articles of food and "dishes" is very different (Rubner). For the method of these investigations and the share which the intestine has in the formation of the fæces, see pages 85 and 96, also Chapter VII.

§ 1. UTILIZATION OF THE FOODSTUFFS

A. PROTEID

We have already seen that the quantity of N in the fæces which comes from the body itself, and therefore represents a product of metabolism, amounts to 0.5–1.4 g. per day. If then we find only this quantity of nitrogen in the fæces after a certain diet, we may say that the ingested nitrogen has all been utilized.

This is generally the case with *animal foods*. In experiments with meat, fish, eggs, milk and cheese, the daily elimination of N in the fæces varies from 0.14 to 1.9 g.; only in one case—with 4,100 g. of milk—do we find in the literature of this subject a greater quantity (3.1 g.) of N in the fæces. If the total N in the fæces be calculated as lost from the N ingested, it amounts to only 2.0–7.7 per cent.

Kermauner has taken the pains to estimate quantitatively the residue of meat recognizable as such in the fæces of three individuals, and has found that after an ingestion of 266 g. meat per day the highest amount in the fæces was 4.7 g. and the lowest 0.3 g. (=0.16 and 0.01 g. N respectively).

With *vegetable foods* the quantity of N in the fæces is considerably greater, and in certain experiments has been known to reach the high value of 9.09 g. per day; the loss in this case amounts to as much as forty-eight per cent and as a rule is more than fifteen per cent.

This is due primarily to the fact that vegetable foods contain nitrogenous compounds in their husks, coats, etc., which are not proteid and are not digested in the intestine. The more husk, etc., a vegetable food contains, the less favorably does the utilization of its nitrogen prove to be. For this reason we find in the fæces from rye bread made from whole meal 2–4 g. nitrogen, representing a loss of thirty to forty per cent. If, on the other hand, most of the bran be removed, the utilization appears more favorable with a loss, namely, of only 2 g. N or ten to twenty per cent. Other factors tending to make the utilization of coarse vegetable foods less favorable are their relative bulkiness, the acid fermentation of the carbohydrates, and the percentage of indigestible substances. All these conditions tend to stimulate the musculature of the intestine and thus to produce a more rapid evacuation of the intestinal contents.

B. UTILIZATION OF FAT AND CARBOHYDRATES

The daily fæces from a diet which contains no fat will lose 3–7 g. by extraction with ether. If, therefore, the fæces after ingestion of a certain fat contain no more fat than this, we can say that that particular fat has all been absorbed from the intestine. This is true of eggs, milk, butter, margarine, lard—in fact, of fats generally which are fluid at the temperature of the body and are not surrounded by membranes. However, even with other fats, like bacon fat, which is inclosed in membranes, the utilization is commonly very complete. Thus, with 350 g. per day, most of which was bacon fat (unrendered lard), only 45 g. appeared in the fæces.

Carbohydrates also are well absorbed in the intestine, inasmuch as the loss by the fæces from the ordinary articles of diet rises only to about ten or eleven per cent at the highest, being as a rule smaller than this. It is true of carbohydrates also that with finely prepared foods the utilization is much better (0.8–3.2 per cent loss) than with coarse foods (6.9–11 per cent loss). The digestibility of cellulose has already been discussed at page 110.

By microscopic examination of the fæces J. Moeller has shown that healthy men digest the starch of cereals and potatoes almost completely, even if the starchy food is but imperfectly ground up. If, however, the starch is present in the form of leguminous seeds or is eaten in green vegetables, it is passed out undigested. The hard-walled cells of the ripe leguminous seeds appear not to be digested at all, so that only that part of the starch which is liberated from the cells by mechanical destruction of their walls is of any benefit in nutrition. The starch of green leguminous plants, on the other hand, is just as completely digested as that of cereals. The gluten layer of the latter behaves like the leguminous seeds: their membranes, consisting of pure cellulose, are not digested, and their contents, consisting of proteid and fat, are digested only so far as they are set free by rupture of the cell membranes.

The absorption of mineral constituents of the diet, calculated in percentages of the amount supplied, is generally rather poor. But we must remember that the ash of the fæces comes mainly from the body itself, seeing that many mineral substances are excreted through the intestinal wall.

C. UTILIZATION OF A MIXED DIET

The experiments which we have discussed so far relate chiefly to the absorption of individual articles of food. We might suppose, however, that a mixed diet, such as is ordinarily eaten by man, would be utilized more advantageously than these experiments indicate; and in fact it has been shown that certain mixtures are absorbed better than their separate components. But all the experiments on the utilization of a mixed diet which we have as yet, go to show that animal nitrogen is absorbed better than vegetable nitrogen.

A few words remain to be added on the *utilization of the total potential energy* of the diet. We assume here as before, that the total fæces represent a residue of the ingested food. For a mixed diet Rubner, on the basis of one experiment on the heat value of the fæces, estimates the loss at 8.11 per cent of the gross calorific value of the food. In those experiments with a mixed diet in which the utilization of all the foodstuffs has been investigated, the results show a loss in potential energy of 4.8 to 13.9 per cent. By direct determinations of the heat value of the food, and of the fæces, Atwater has found in 117 experiments with a mixed diet of easily digestible substances, that the loss of potential energy was from 2.6 per cent to 11.7 per cent. In this important series the loss in proteid was 3.8 to 11.7 per cent, in fat 1.7 to 12.7 per cent, in carbohydrates 0.9 to 5.2 per cent.

An average figure to express the utilization of energy in the food ought not be placed too low. Suppose we assume that ten per cent of the potential energy is lost, then to supply a man with 3,000 Cal. his diet should have an indicated value of 3,333 Cal. Because of the many analyses necessary, a complete experiment on the utilization of foods in the intestine is attended by considerable difficulties. But for all practical purposes it is sufficient to determine the dry residue of the diet and of the corresponding fæces; for the percentage loss in dry substance, so far as our experience yet goes, varies but slightly from the percentage loss in energy.

§ 2. THE ENERGY REQUIREMENTS OF AN ADULT

It is already clear that the requirements of an adult must be determined essentially by the physical work to be done, for work is inseparable from a consumption of substance. Hence we have first to investigate how great the total supply must be for different amounts of work. The problem is simplified materially by excluding the inorganic foodstuffs, for it has been shown that if the diet is sufficient and has the proper constitution in other respects, it will contain also plenty of inorganic substances.

To determine the minimal requirement, observations must be made on the metabolism in complete muscular rest. Such observations have given the following results:

A woman, twenty-five years of age, weighing 49.5 kilograms, who was in an hysterical sleep and ate nothing, excreted in twenty-four hours 6.21 g. N and 107 g. C = 38.8 g. proteid and 113.2 g. fat, corresponding to 1,228 Cal., or 1.03 Cal. per kilo per hour.

In his calorimetric experiments Atwater obtained as a mean of sixteen determinations of the heat loss in sleep (from 1 A. M. to 7 A. M.), the value of 1.03 Cal. per kilo per hour.

The minimal requirement of the adult man may be placed, therefore, at 1 Cal. per kilo per hour—i. e., for a man of 70 kg. 1,680 Cal.

But for patients in a weak bodily condition muscular rest so complete as this never occurs. The skeletal muscles are always moved to a greater or less extent; hence metabolism must be somewhat greater than in sleep.

The experiments of Pettenkoffer and Voit on individuals at rest give an average (for twenty-four hours) of 2,303 Cal. in fasting and 2,675 Cal. on a moderate diet—i. e., 32.9 and 38.2 Cal. respectively per kilo per day. In experiments by Sondén and the author on eight resting men between the ages of nineteen and forty-four years, the metabolism varied from 1,853 to 2,292 Cal., or from 26.3 Cal. to 36.0 Cal. per kilo per day. Eckholm's results on ten students and thirteen soldiers between nineteen and twenty-five years gave a mean result of 35.6 and 37.0 Cal. respectively. From Atwater's calorimetric experiments carried out on three different subjects and covering forty-five days, we get a total metabolism for the resting man of 2,241 Cal.—i. e., 32.9, 33.3, and 33.4 Cal. per kilogram.

The metabolism of a grown man, who neither rests absolutely, nor does any real physical work (providing he receive not too limited a supply of food), may be estimated, therefore, at 30–36 Cal. per kilogram per twenty-four hours—i. e., for a body weight of 70 kg., 2,100 to 2,520 Cal. Consequently a ration which does not supply at least 2,000 Cal. net (i. e., allowing ten per cent waste; cf. page 140) must be declared insufficient for a physical laborer.

Laborers' rations may be divided, according to the amount of energy required, into several different groups. The following is arranged especially for men:

GROUP.	Calories (net).	Sufficient for a	Climate.
I.	2,001–2,400	Shoemaker.	England.
II.	2,401–2,700	Weaver.	Saxony.
III.	2,701–3,200	Soldier.	Germany.
IV.	3,201–4,100	Farm laborer.	Scotland.
V.	4,101–5,000	Excavator.	France.
VI.	Over 5,000	Lumberman.	Bavaria.

The following may be given as examples of rations which would yield an average supply of energy sufficient for each of these classes:

GROUP.	Proteid, gross g.	Fat, g.	Carbohydrate, g.	Calories, gross.	Calories, net.	Calories per kg. body weight (mean = 70 kg.).
I	84	56	399	2,483	2,235	32
II	88	39	512	2,825	2,538	36
III	130	64	520	3,257	2,932	42
IV	141	71	677	4,020	3,618	52
V	167	89	774	4,685	4,218	60
VI	152	139	1,062	6,269	5,642	81

Within the last few years a large number of observations on the nutrition of men who had free choice of their own food, have been made under Atwater's direction in the United States. The results are recorded in the following table:

GROUP.	Cal., net.	Number of observations.	Proteid, gross; g.	Fat, g.	Carbohyd., g.	Cal., gross.	Cal., net.	Cal. per kg., b. w. (70).
I.	2,001–2,400	23	87	90	303	2,434	2,191	30
II.	2,401–2,700	15	89	112	362	2,891	2,602	37
III.	2,701–3,200	37	103	125	409	3,262	2,936	41
IV.	3,201–4,100	35	124	147	510	3,966	3,569	51
V.	4,100–5,000	14	145	215	612	5,102	4,592	66

Voit based his practical conclusions for the nutrition of an adult man on the requirements of a moderate worker. He describes as a " moderate worker," a man strong enough to do nine to ten hours' work every day heavier than that of a tailor and lighter than that of a blacksmith—the work for example of a mason, a carpenter, or a joiner. Moderate work so defined corresponds fairly well to the amount done by most manual laborers, and comes nearest to Group III in our classification.

Voit's ration for the moderate worker is: 118 g. proteid, 56 g. fat, and 500 g. carbohydrate = 3,055 Cal. gross or 2,749 Cal. net.

While it has been generally admitted that the absolute supply of energy in this ration corresponds well with the actual requirements and is estimated rather too low than too high, it has been remarked by many that the amount of proteid is too high and that a moderate worker can get along perfectly with less proteid. Munk for example proposes 110 g. proteid instead of 118 g. Now it is not a matter of great moment whether the diet contain 110 or 118 g. proteid. The rations which we have brought together for our Group III contain on the average 130 g. with 113 and 151 g. as the extremes. From Atwater's results we have for the same group 103 g. with 52 and 152 g. as the extremes. This is not the place to discuss the grounds which have been taken for a reduction of proteid in the ration. In the opinion of the author these grounds are by no means sufficient for the purpose intended, hence the best thing to do is to choose for a normal ration on containing not less than 118 g. proteid, even is many observations do show that a "moderate worker" can *get along* with less.

[Chittenden's recent experiments on several groups of men of different degrees of muscular and mental activity (university professors, college athletes, and United States soldiers) indicate strongly that Voit's proteid ration is excessive. He found that without exception these persons (numbering twenty-six in all) were able to maintain their physical and mental vigor for periods of from five to nine months on an average of 56 grams of proteid per day. These results accord with Folin's theory of metabolism (cf. page 137), which looks upon a large part of the proteid ingested in the average diet as so much waste material to be removed at once from the circulation by the liver.—Ed.]

Voit's motive in dividing the nonnitrogenous foodstuffs for a moderate worker between fat and carbohydrates as he did, was to make the diet as inexpensive as possible. He takes, therefore, as much carbohydrate as in his opinion the intestine can digest easily—i. e., 500 g. The remainder of the energy required he takes from fat.

Of course it would not be correct to regard 500 g. as a real maximum of carbohydrates—and Voit does not. The intestine can manage greater quantities; but this alone is no reason for increasing the carbohydrate at the expense of fat. Experience has shown with perfect clearness that the human body has a very pronounced, if not always a perfectly intelligible, need for fat; so that the quantity in Voit's ration (56 g.) ought probably to be regarded as the minimum for the diet of a moderate worker (cf. tables on page 141).

When the amount of work to be done is greater than that of a moderate worker, experience teaches us that both proteid and N-free substances are eaten in greater quantities, but the supply of proteid is not increased as much as that of the N-free substances. According to Voit, soldiers in field maneuvers (hard labor) require 135 g. proteid, 80 g. fat, and 500 g. carbohydrates = 3,348 Cal. gross and 3,013 Cal. net, and in war (severe labor) 145 g. proteid, 100 g. fat and 500 g. carbohydrate = 3,575 Cal. gross and 3,218 Cal. net.

Our Group IV contains on the average 3,618 Cal. net which can be supplied in 141 g. proteid, 71 g. fat, and 677 g. carbohydrates. We see that this ration agrees on the whole very well with that demanded by Voit. For a similar class (3,569 Cal.) Atwater (IV) finds 124 g. proteid, 147 g. fat, and 510 g. carbohydrates to be the requirement.

The following data by Atwater may be given as further examples of diets suited to severe labor: Participants in a rowing contest (American students): 155 g. proteid, 177 g. fat, 440 g. carbohydrates = 4,085 Cal. gross. Football players: (1) 181 g. proteid, 292 g. fat, 557 g. carbohydrates = 5,740 Cal. (gross); (2) 270 g. proteid, 416 g. fat, and 710 g. carbohydrates = 7,885 Cal. (gross).

Direct information on the *diet of women* is still extremely meager. Having a smaller body than man, and doing as a rule less physical work, a woman naturally requires a smaller supply of energy than a man. Assuming that the weight of the woman's body is four-fifths that of the man's and that her metabolism bears the same relation to his, we obtain Voit's ration for female workers: 94 g. proteid, 45 g. fat and 400 g. carbohydrates = 2,444 Cal. (gross) and 2,200 Cal. (net).

§ 3. NUTRITION OF THE YOUNG

It is evident that the growing body needs relatively more food than the adult, both because it is smaller and because its organs must increase in size. Moreover, experiment has shown that the young body has a more active metabolism per *unit of body surface* regardless of its smaller size (page 118).

In order to make possible a fuller presentation of the metabolism in the growing body, we have brought together in the following table a number of observations on the mean CO_2-output taken a short time after a meal while the individuals were sitting quiet. Still other data will be found on page 119:

Males.			Females.		
Age, years.	Mean Bodyweight, kg.	CO_2, g. per hour.	Age.	Mean Bodyweight, kg.	CO_2, g. per hour.
9¾	28	33	8	22	25
10½	30	33	10	27	23
11½	32	34	11	31	26
12½	34	34	12	36	27
14	45	45	13	40	28
14½	45	44	14	44	29
15½	51	42	15	49	27
17	56	45	16	50	32
19½	60	43	17⅔	54	27
23	65	38	30	54	29
25	68	38	45	67	37
35	68	35	65¾	67	26
45	77	37			
58	85	34			

With *males* we see that the excretion of carbon dioxide is greater between the ages of fourteen and nineteen than in older or younger individuals of the same sex. This agrees very well with Key's observation on the growth of boys, namely that beginning with the fourteenth year the increase of the body in length and weight takes place much more rapidly than during the years immediately preceding (nine to thirteen). This period of rapid growth continues for four years (cf. Chapter XXVI, second section).

To judge by the elimination of CO_2, a boy from nine to thirteen, therefore, would need almost as much food as a man resting, and boys between fourteen and nineteen still more. We must not overlook the fact, however, that the calorific value of the CO_2 is very different according as it has its origin in the metabolism of fat, carbohydrates or proteid. Since in the above table the individuals on whom the experiments were made belonged to the same class of society, and so far as the diet, etc., were concerned lived on the whole on the same plane, it may be assumed with great probability that the average composition of their diet, and consequently the share of the different foodstuffs in the formation of CO_2, was about the same.

With *females* the CO_2-elimination does not show the significant rise which appears in boys between fourteen and nineteen. From the eleventh year on but slight differences due to age make their appearance: in an eleven-year-old girl the CO_2-excretion was 26 g., in a woman of thirty, 29 g. We might say, therefore, that the requirements of a girl of eleven are just as great as those of an adult woman at rest.

Comparison of the CO_2-output of males and females of the same weight and age shows that during the years of growth it is considerably greater with the former than with the latter, and that the ratio of female metabolism to male metabolism estimated per kilogram of body weight is about 100:140. In men and women who have already passed the period of growth this difference gradually diminishes, and as old age comes on disappears altogether.

The figures of this table differ considerably from those given by Magnus-Levy and Falk in the table on page 118. The reason is that the subjects of their experiments had not eaten recently and were in absolute muscular rest, while the results brought together in the table now under consideration were obtained upon individuals in a sitting posture shortly after a meal. On this account Magnus-Levy and Falk found no difference in the CO_2-excretion by males and females. The difference which we have noted above is, in all probability, traceable to a greater tonus in boys' muscles than in girls'.

By way of comparison with the direct data on the metabolism of the growing body we may add also the standard figures which Atwater uses in apportioning the diet of a family to its different members. Taking the food requirements of the father as 1, the requirements of the others would be:

Of the mother	0.8;
“ sons, 14–17 years	0.8;
“ daughters, 14–17 years	0.7;
“ children, 10–13 years	0.6;
“ “ 6–9 years	0.5;
“ “ 2–5 years	0.4;
“ “ under 2 years	0.3.

§ 4. CONSTRUCTION OF THE DIET FROM THE DIFFERENT ARTICLES OF FOOD

In satisfying the requirements of his body, man has a great variety of foods, both animal and vegetable in origin, from which to choose. Recently the question has been much discussed in certain quarters whether the natural food of man should be mixed or should be purely vegetable.

That a purely *animal diet* is not suited to the requirements of the human body after the period of infancy is passed need not be proved at length. On the one hand, if we except milk and liver, the carbohydrates are practically absent entirely from such a diet; and on the other hand, the relatively long human intestine is not sufficiently stimulated by an exclusively animal diet to prevent the residues of the food and the digestive fluids from remaining overlong in the intestine.

All the requirements of the body can be met, however, by foods of *vegetable origin* alone; for they contain fats and carbohydrates as well as proteid.

Vegetarians assume that a purely plant diet is the only natural food of man. But a number of objections can be raised against this conception. For example, fat occurs in plants in large quantities only in the form of vegetable oils, and the only place the latter figure to any extent in the preparation of victuals is in southern countries. Hence, in many regions it is not easy on a purely vegetable diet to supply the body with a sufficient quantity of fat. To obtain fat the body must appropriate animal foods. Again, most vegetable foods in proportion to their percentage of proteid are much more bulky than animal foods, and their volume is still more increased by the absorption of water in their preparation, whereas animal foods lose water in preparation and hence become less bulky. Besides, the nitrogenous constituents of most vegetable foods are but poorly absorbed in the intestine. In order to supply the body with plenty of proteid from purely vegetable sources one is compelled, therefore, to eat a rather voluminous diet. In so doing he runs the risk of exacting too much work of the digestive organs, whence various untoward effects might result. To prevent these, it is needful that a part of the daily ration be drawn from animal sources.

This is admitted by the vegetarian who eats no meat, but allows himself the pleasure of milk, eggs and dairy products. In his case the diet is no longer purely vegetable, for it contains both fat and proteid derived from animal sources. Cheese is an article very rich in proteid, and in butter and milk the body can get all the fat it requires. So far as the question is debatable at all, it narrows itself to whether or not meats shall be included in the diet.

From a purely physiological point of view, we can find no reason why a healthy man should forego the use of so excellent an article of food, considered with respect to its content of proteid and fat or its eminent adaptability, as we know meat to be. But in so stating, I do not wish to be understood as saying that one should eat any quantity of meat he pleases, or should cover too much of his requirements with meat. In too large quantities the extractive substances found in meat may possibly produce disorders of one kind or another in the body (cf. Chapter XII, § 1). The metabolism might also take an abnormal or unfavorable form, if the fluids of the body were flooded with too much proteid. Finally, it is possible that in certain diseased conditions, meat would be harmful, and that some persons have a positive aversion to it.

If, therefore, the individual get a sufficient supply of proteid and fat in other articles of diet, like cheese and butter, so that great bulkiness can be avoided, meats are not absolutely necessary. But from the standpoint of the physiology of nutrition, there is no reason for avoiding them.

Against the claim that the vegetable foods constitute the natural—i. e., the original diet of man—this additional objection can be raised: the most important of the vegetable foods, namely the cereals, are subject to the action of the digestive fluids only after thorough preparation; whereas man had lived a long time on the earth before he had progressed so far as to understand how to cultivate the soil, cook his food, grind his grain and bake bread. Meat, however, requires no further preparation for eating than to be divided into small pieces. We have reason, therefore, for claiming rather that man was originally carnivorous.

There are those who would have us believe that the really natural diet of man consists of fruits. But it is not a very easy matter at best to get proteid and fat enough from fruits, and besides, in many inhabited lands it is quite impossible to raise any fruits or any kind of vegetable foods in large enough quantities to provision the population.

Our conclusion is that the diet most generally suitable for man is a mixed diet, composed of both animal and vegetable foods. It is only by reason of his ability to utilize all sorts of foods that it has been possible for man to people the entire earth from the equator to the poles.

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CHAPTER V

THE BLOOD

The blood is the common nutritive fluid of the body. Driven by the heart through the vascular system in an uninterrupted stream, it supplies all parts of the body with all the substances necessary for their growth and maintenance, as well as for the combustion going on in them. Besides, the blood removes from all parts of the body the greater part of the decomposition products formed in the life processes, and is in its turn relieved of these products during its passage through the excretory organs.

The blood is a red, opaque fluid, somewhat heavier than water (sp. gr. in man 1.057–1.066, in woman 1.053–1.061). It has a salty taste, a neutral reaction, and a peculiar, stale odor. Its specific heat amounts to 0.8693 (at about 38° C.).

The blood holds its neutral reaction with the greatest tenacity. In order to obtain a red coloration with phenolphthalein by addition of caustic soda to the serum of ox blood, one must add seventy times as much of the alkali as would be necessary if it were being added to pure water in order to obtain the same reaction. The same serum mixed with methyl-orange requires three hundred and twenty-seven times as much n/10 HCl as does pure water in order to bring out the red coloration. The explanation of this behavior lies in the variable acid and basic character of the serum proteids (Friedenthal).

On microscopic examination the blood is found to consist of a fluid, the plasma, in which float great numbers of formed elements. These latter constituents which cause the opacity of the blood are: (1) the *red blood corpuscles* to which the blood owes its red color; (2) the *white corpuscles*; (3) the *platelets.*

A few minutes (in man three to twelve) after the blood is drawn from an open blood vessel it sets into a jellylike mass, which, as will be more fully discussed later, is due to the fact that a proteid body present in the plasma is separated out (coagulated) in the form of a solid, the so-called *fibrin.*

The coagulated fibrin is a fibrous structure, which, although it amounts to only 0.2–1.0 per cent of the blood, permeates and incloses in its meshes the entire mass of the clot. Gradually the fibrin shrinks, in consequence of which a pale yellowish fluid is pressed out. The quantity of this fluid, the *serum,* increases progressively and finally there remains of the coagulum a smaller residual mass, which consists of the fibrin, the blood corpuscles inclosed in it, and the serum still present in its interstices. The blood plasma therefore consists of fibrin and serum.

Fibrin may be separated out also by whipping shed blood with a stick. After this operation the blood remains fluid, the fibrin having been collected in the form of a white, stringy mass on the stick.

§ 1. THE AMOUNT OF BLOOD IN THE BODY

The method of determining the amount of blood in the body is in brief as follows: a normal sample of blood (b) is first drawn; then the animal is bled and the vascular system is washed out with water until the water flows out perfectly clear. The water and blood are added together and the total quantity designated w. The normal sample of blood is now brought by addition of water v to the same color as a sample of w. Then if we designate by y the amount of blood washed out, it is evident that $b : b + v :: y : w$. From which $y = \frac{b \times w}{b + v}$ The total quantity in the body is therefore $b + y = b + \frac{b \times w}{b + v}$ (Welcker). This method is not, however, quite exact, for after the washing there still remains in the organs from eight to sixteen per cent of the total hæmoglobin.

The amount of blood determined in this way amounts to seven to nine per cent of the body weight in the dog, five to nine per cent in the rabbit (in the latter after removal of the intestinal contents). Bischoff found in the dead bodies of two executed criminals the quantities 7.1 and 7.7 per cent of the body weight.

§ 2. THE FORMED CONSTITUENTS OF THE BLOOD

A. THE RED BLOOD CORPUSCLES

In most mammals the red blood corpuscles are thin, flat, slightly biconcave, circular disks, composed of a soft, extensible and very elastic substance. By transmitted light the color in thin layers is yellowish green; in thick layers, red. In birds, reptiles, amphibia and most fishes, as well as in the camel family, they are oval instead of circular. In the cold-blooded animals and in birds they have a nucleus: in the mammals no nucleus is present in the mature form of the corpuscle (cf. page 17).

The diameter of the red blood corpuscle in man is 0.007–0.008 mm., its thickness about 0.0016 mm. The volume of a single corpuscle, according to Welcker, amounts to 0.000000072 cu. mm., and its surface to 0.000128 sq. mm. One cu. mm. of human blood contains about 5,000,000 red corpuscles for man and about 4,500,000 for woman. The total surface of the red corpuscles in 1 cu. mm. of blood therefore amounts to 640 sq. mm. in man and 576 sq. mm. in woman. Since the total mass of the blood in man is about seven per cent of the body weight, i. e., in a body weighing 70 kg., about 5 kg. in round numbers, the total number of red blood corpuscles in a man is 25,000,000,000,000, and their total surface 3,200 sq. m. (= 0.8 acre nearly).

(The body surface of a grown man is only about 2 sq. m.) This enormous extent of surface of the red blood corpuscles is of great significance in connection with their function in respiration (Chapter IX).

Moreover the number of red blood corpuscles in 1 cu. mm. of blood varies not a little under perfectly normal circumstances. Some authors have observed an increase, others a decrease in the number after meals. There is substantial agreement, however, that complete or partial abstinence from food does not reduce the number. Rarefaction of the air, as on mountain tops, increases the number of red corpuscles per cubic millimeter of blood very considerably, and the effect is not due to an excessive elimination of water from the body, for the same thing has been noted on animals where an increased transpiration of water was impossible. The increase has been regarded as an attempt on the part of the organism to offset incomplete saturation of the blood with oxygen, resulting from lower air pressure. But this explanation does not suffice, for the increase takes place just the same before the reduction of pressure is sufficient to affect the absorption of oxygen.

It should be remarked in connection with these and other normal variations in the number of red blood corpuscles, that blood-counts give us only the relative number, and do not throw any light on the total number of corpuscles. For it must not be forgotten that under some circumstances the relative number of corpuscles in different parts of the body varies greatly (Zuntz), nor that an exudation of plasma from the vessels may produce an apparent increase (Bunge)—in short, it is not an easy matter properly and exactly to estimate the total number of blood corpuscles.

The *specific gravity* of the red corpuscles (1.008–1.105) is greater than that of the plasma or of the serum (the sp. gr. of the latter in man amounts to about 1.017). Hence they sink to the bottom of a vessel in which the blood is caught, provided we are dealing with whipped blood, or blood whose coagulation is artificially stopped or retarded. Since the separation of the blood corpuscles from the plasma or serum can be accomplished much more rapidly with the centrifuge than by mere settling, this instrument is often used in blood work.

On the addition of very small quantities of most acids or acid salts of Fe, Al, Zn, Cu, Hg, Sn, Ag, Au, Ur, Mb, the red blood corpuscles become agglutinated, and thereby precipitated. The same takes place even with hæmoglobin-free stromata as well as with the leucocytes, and is probably caused by an effect on the contained globulin (Peskind).

The weight of the red blood corpuscles in 100 parts of blood is estimated, according to Alex. Schmidt, in the following manner: (1) The percentage of dry residue (T) in the whole blood is determined; (2) the percentage of dry residue (t) in the serum belonging to this quantity of blood; (3) the dry residue (r) of the red blood corpuscles obtained from 100 g. of blood. The dry residue of the serum obtained from 100 g. of blood is then $\mathrm{T}-r$, and the corresponding quantity of serum is $\frac{100 \times (\mathrm{T}-r)}{t}$, so that the *weight of the red blood corpuscles* in 100 parts of blood is $100 - \frac{100 \times (\mathrm{T}-r)}{t}$.

By this method it has been found that the *weight of the corpuscles in 100 g. of defibrinated blood is 48 g.* (mean of nine observations) *for the man and 35 g.* (mean of eleven observations) *for the woman.*

The red blood corpuscles are continually going to pieces in the body in great numbers, especially, as it appears, in the liver. Naturally there is, under normal conditions, a corresponding production of new ones. In embryonic life the liver and spleen play a prominent part in their formation. In the adult, according to most authors, red blood corpuscles are formed only in the red marrow of the bones. (For the importance of Fe in the formation of hæmoglobin, see Chapter VIII.)

The blood corpuscles owe their red color to the pigment substance *hæmoglobin,* whose chemical properties were first closely investigated by Hoppe-Seyler. It unites with oxygen into a compound called *oxyhæmoglobin,* the amount of which depends (to some extent) upon the partial pressure of the available oxygen. The hæmoglobin in the arterial blood occurs chiefly in this form; in venous blood hæmoglobin as well as oxyhæmoglobin is found; but in *asphyxiated blood only hæmoglobin.*

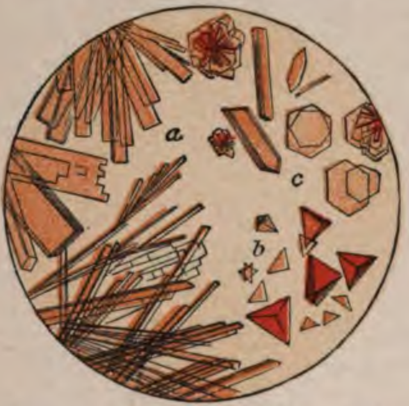

FIG. 46.—Blood crystals, after Funke. *a,* from the human blood; *b,* from the blood of the guinea pig; *c,* from the blood of a squirrel.

By thinning with water, by repeated freezing and thawing, by addition of ether, chloroform or bile, or of acids or bases, the coloring matter may be washed out of the corpuscles and brought into solution. The blood is then said to be of a *laky color,* or is *laked.* In many cases the passage of the hæmoglobin out of the corpuscle does not run parallel to the outward diffusion of the electrolytes. Under certain circumstances the hæmoglobin passes out while the electrolytes remain behind. Under others the opposite takes place: the electrolytes leave the corpuscle and the hæmoglobin remains. This shows that the mode of combination of the hæmoglobin and of the electrolytes is somewhat different (Stewart).

According to Hoppe-Seyler neither the hæmoglobin nor the oxyhæmoglobin is present as such in the red corpuscle, but as a tolerably firm combination with another substance, probably lecithin. The combination which contains oxyhæmoglobin is called *arterin,* while that of which hæmoglobin is a constituent is known as *phlebin.*

After the coloring matter is dissolved out of the red blood corpuscles there remains a colorless mass called the *stroma.* This consists of lecithin, cholesterin, proteids, urea, and mineral substances, chiefly potassium, phosphoric acid and chlorine, and in the red blood corpuscles of man, sodium.

By far the greatest part (eighty-seven to ninety-five per cent) of the dry substance of the red blood corpuscle consists of hæmoglobin: the stroma of the blood corpuscles amounts therefore to only five to thirteen per cent. In the blood of a man there is found 13.8 per cent hæmoglobin, and in that of a woman 12.6 per cent.

The quantity of hæmoglobin in the blood shows great variations under different circumstances, and as a rule, though not always, it varies directly as the number of corpuscles. The quantity of hæmoglobin in proportion to the body weight is greatest in the newborn and sinks rapidly during the first few days after birth—e. g., in the rabbit in twenty-two days, it sinks from about 13 g. to 4 g. per kg. of body weight. During this time the absolute quantity of hæmoglobin increases and the iron stored up in the body in other forms decreases (Abderhalden).

Oxyhæmoglobin crystallizes out of its solution more or less readily. The crystals (Fig. 46) are blood red, are transparent, and belong, whatever their form, to the *rhombic system* (Lang). From fresh human blood one may obtain three forms of crystals, namely: (1) large, scalariform plates, (2) sharply defined, dark red, doubly refractive, four-angled prisms, and (3) sharply defined rods much split up at the ends (Frieboes). Only the oxyhæmoglobin of the squirrel (Fig. 46 *c*) crystallizes in six-sided tablets of the hexagonal system.

Hæmoglobin is distinguished from oxyhæmoglobin chiefly by being more easily soluble, and more difficult of crystallization, although the two are as a rule isomorphic. The crystals and the water solution of hæmoglobin are darker, more violet, or purple colored than the crystals and the solution of oxyhæmoglobin. In thin layers hæmoglobin is greenish, in thicker layers red. Oxyhæmoglobin solutions are always red whatever the thickness. Finally, the two show noteworthy differences in their absorption spectra, as will be evident from Figs. 47 and 48. If the solution is not too concentrated the absorption spectrum of oxyhæmoglobin shows two bands α and β between the D and E lines. With weaker solutions the β band disappears first. The more concentrated the solution is, however, the broader the bands become until finally they fuse together, whereby the blue and the violet parts of the spectrum are at the same time more and more obscured. The absorption spectrum of hæmoglobin on the contrary shows a single broad band between the D and E lines, but nearer the D.

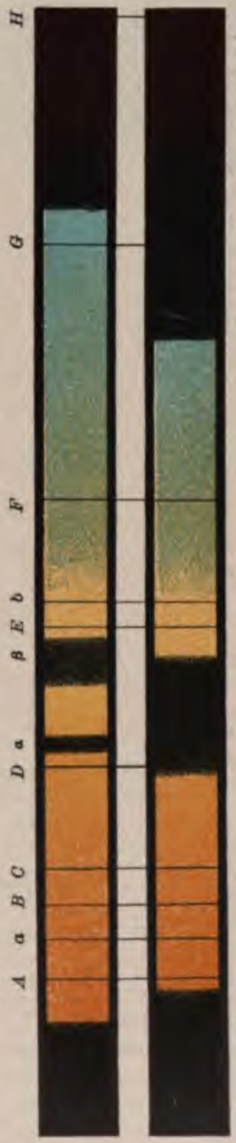

FIG. 47.—Absorption spectrum of a 0.09 per cent solution of oxyhæmoglobin, after Preyer.

FIG. 48.—Absorption spectrum of a 0.2 per cent solution of hæmoglobin, after Preyer.

In *methæmoglobin* oxygen occurs in the same quantity as in oxyhæmoglobin, but is more firmly united. There is also a compound of hæmoglobin which contains less oxygen than the oxyhæmoglobin, but is not completely reduced like the hæmoglobin. It is called ***pseudohæmoglobin*** and has the same absorption spectrum as hæmoglobin (Siegfried).

Hæmoglobin unites with still other substances, as carbon monoxide (***carbon-monoxide hæmoglobin***) a compound corresponding to oxyhæmoglobin but more stable, with carbon dioxide (*carbon-dioxide hæmoglobin*, cf. Chapter IX) and nitric oxide (*nitric-oxide hæmoglobin*).

From analytical data Hüfner has calculated the following formula for the hæmoglobin of the dog's blood: $C_{636}H_{1025}N_{164}FeS_3O_{181}$ (molecular weight = 14,129).

In different animals hæmoglobin has a somewhat different constitution: for the hæmoglobin of the dog, horse, swine, guinea pig, and squirrel various authors have found the following constitution: C 51.2–54.9 per cent, H 6.8–7.4 per cent, N 16.1–17.9 per cent, S 0.39–0.86 per cent, Fe 0.34–0.59 per cent, O 19.5–23.4 per cent.

For every molecule of hæmoglobin contained in oxyhæmoglobin there is one molecule of oxygen—i. e., for 1 atom of iron, 2 atoms of oxygen. From this it can be shown that 1 g. of hæmoglobin can absorb 1.34 c.c. of oxygen. The dependence of the oxygen absorption by hæmoglobin upon partial pressure will be discussed more fully in Chapter IX.

Hæmoglobin is a conjugated proteid (cf. page 75) in which a simple proteid is coupled with an iron-containing pigment, *hæmochromogen* (Hoppe-Seyler). In 100 parts of hæmoglobin there are 94 parts proteid and 4 parts coloring matter. The former consists for the most part of a histon-like basic body, globin (Schulz), which like other simple proteids is lævorotatory, while hæmoglobin itself is dextrorotatory (Gamgee and Croft-Hill).

On cleavage of hæmoglobin, hæmochromogen is formed, and by absorption of oxygen it passes over into *hæmatin*: $C_{34}H_{34}O_5N_4Fe$ (Küster), $C_{34}H_{35}O_5N_5Fe$ (Zeynek). By treatment of the blood pigment with HCl, *hæmin* is obtained (Fig. 49): $C_{32}H_{32}O_3N_4FeCl$ (Nencki).

Acids change hæmatin by loss of iron into the pigments ***mesoporphyrin***, $C_{16}H_{18}O_2N_2$ (Nencki) and *hæmatoporphyrin*, $C_{16}H_{18}O_3N_2$ (Nencki). Energetic reduction of the latter yields an oily, oxygen-free substance, ***hæmopyrrol***, $C_8H_{13}N$ (Nencki), which according to Nencki and Zaleski is either an isobutyl pyrrol or a methyl-propyl pyrrol.

Hæmatoporphyrin is only slightly different from a chlorophyll derivative, *phylloporphyrin* $C_{16}H_{18}ON_2$, prepared by Schunk and Marchlewski. This fact which indicates a close agreement between the structure of the most important coloring matter of plants, and that of the most important coloring matter of animals suggested to Nencki and Marchlewski the possibility of obtaining identical products from the two. They succeeded in producing hæmopyrrol from chlorophyll. In view of the importance of pyrrol in the molecule of both hæmoglobin and chlorophyll, we may conclude that the two are in fact very closely related.

B. THE WHITE CORPUSCLES

These are colorless, nucleated cells. Some varieties of them, at least, have, *like the free-living amœbæ*, the power to move independently from one place to another by the protrusion of pseudopodia. On account of this very remarkable property they probably play a very important rôle in many processes of the body, although this rôle is not yet sufficiently well known. Their activity is entirely independent of the nervous system and is controlled, in great part at least, by chemotactic influences (cf. page 54). Their general function, so far as investigation has yet been able to determine, *is to provide for the transportation of various substances inside the body and to destroy or to remove foreign substances from the body.*

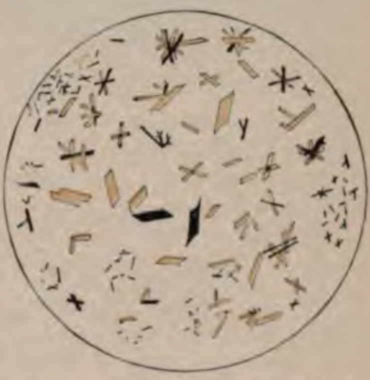

FIG. 49.—Hæmin crystals, after Preyer.

The number of white corpuscles shows considerable variation under normal circumstances, a fact dependent in part at least on their entrance into or withdrawal from the blood stream in greater or less numbers. (Concerning the multiplication of white blood corpuscles appearing in digestion cf. Chapter VIII.) In the adult the average number is 8,000 to 9,000 per cu. mm.—i. e., one white to every 500 to 600 red corpuscles. In the newborn the leucocytes are much more numerous and reach on the average 18,000 per cu. mm.

The white corpuscles are formed in extrauterine life chiefly in the spleen and lymphatic glands: from these issue mononuclear cells (*lymphocytes*) which, according to some authors, are transformed into polynuclear cells in the blood stream. Moreover they exhibit a variety of forms and are divided according to their appearance and staining reactions into several groups (see text-books of histology).

C. THE BLOOD PLATELETS

Discovered by Hayem (1877) and demonstrated in the circulating blood by Bizzozero and Laker, the blood platelets are spherical or ellipsoidal bodies which send out in all directions processes of variable number and length, composed of the same shiny material as the body. According to the investigations of Deetjen, Dekhuyzen and others, they have the full value of cells, consist of nucleus and protoplasm, and are capable of amœboid movement. Their size varies between 0.005 and 0.0055 mm. Their number, according to Brodie and Russel, amounts to about 635,000 in 1 cu. mm. of blood. With respect to their chemical constitution it is especially emphasized that they contain a nuclein body coupled with proteid; and with respect to their physiological purpose it is assumed by several authors that they play an essential part in the coagulation of the blood. Their origin is as yet conjectural.

§ 3. THE PLASMA

As already mentioned on page 147, the blood coagulates a few minutes after it has left the body, and before a separation of the plasma from the blood corpuscles can take place. Coagulation may be postponed by chilling the blood to 0° C. Then on account of their greater weight the corpuscles sink to the bottom and (especially with horse's blood) a plasma entirely free of corpuscles may be obtained for study. Most investigations on the fluids of the blood relate however to the *serum*, which is distinguished from the plasma chiefly by the fact that it contains no fibrinogen and less ash, because the fibrin when it separates out carries down with it either mechanically or in chemical combination, some of the ash constituents.

A. CHEMICAL CONSTITUTION OF THE PLASMA

Both plasma and serum are clear, faintly yellow fluids with a specific gravity of about 1.028. The specific heat of serum is 0.9401, greater therefore than that of the whole blood.

Besides water, plasma contains chiefly proteid substances of different kinds, and mineral constituents. The osmotic tension of plasma is about equal to that of a 0.9 per cent NaCl solution and is dependent mainly on its mineral constituents. The proteid bodies also appear to influence this property, though only to a relatively slight extent.

The mineral constituents in the serum are dissociated into their ions to the extent of about seventy-five per cent (Bugarsky and Tangl); while in the whole blood, electrolytic dissociation amounts to only about forty per cent (Oker-Bloom).

The electrical conductivity of the whole blood is less than that of the serum, because this property is diminished by the presence of the corpuscles, as in general the conductivity of a solution is diminished by nonconducting particles in suspension (Bugarsky and Tangl, Oker-Blom, *et al.*).

The mineral substances in the serum differ essentially from those in the corpuscles, in that sodium salts predominate in the former, potassium salts in the latter. Among the sodium compounds, common salt occurs in greatest quantity (about 0.6 per cent). Besides this, various other inorganic substances have been found in the serum. On the whole the mineral substances in the serum of human blood amount to about 0.85 per cent.

The organic substances in the serum amount to about ten times as much, namely, 7.7–9.0 per cent. Among these the proteids are the most important and make up by far the greatest part of the organic matter (about nine-tenths). The chief proteids of the blood plasma are fibrinogen, serum globulin and serum albumin. The latter two however are not to be regarded as indivisible substances; for numerous investigations in recent years have shown, if one may judge by their behavior in salting out, that at least two, probably several, globulins (euglobulin, pseudoglobulin) are present in the blood (cf. page 74); and, according to results of fractional heat coagulation, that serum albumin also is a mixture of different proteid substances.

Besides the proteids we find in the blood: *fats* (and the cholesterin ester of fatty acids, but as a rule no free cholesterin, Hürthle); *glycerin* and *carbohydrates* (sugar, probably for the most part in combination with lecithin as jecorin: Jacobsen, Henriques, Bing); also substances which are formed in the activity of the tissues and either represent *decomposition products* to be given off from the body (like urea, uric acid, creatin, carbamic acid, paralactic acid, hippuric acid, etc.) or are formed for the purpose of influencing the functions of different organs (*internal secretions*, cf. Chapter XI)—in short, everything which the tissues have need of for their activity, and most of the products arising from this activity.

With the exception always of the proteids, these substances occur in very small quantities in the blood. In the intervals of digestion one finds from one to seven per cent of fat in the serum, while during digestion it mounts much higher. Even in starvation (one hundred and twenty hours after food has been taken) the fat content of the blood is higher than in the inanitiate condition (twelve hours after the last meal)—a fact connected with the movement of the body's fat for the purpose of covering the food requirements (Schulz). In the healthy condition the sugar content of the serum amounts to about 1–1.5 per cent, but after very abundant feeding of carbohydrates may increase to three per cent and higher. The maximum urea content is about one per cent, etc. These quantities appear at first sight to be astonishingly small, but they become intelligible when we reflect that the blood is in continual motion and its contributions of fat and carbohydrates to all the tissues are continually being replaced from the great storehouses of the body. In the same way it takes up the decomposition products from the tissues, and continually eliminates them by way of the excretory organ so that under normal conditions it contains at any given time a very small quantity of these substances also.

Various *enzymes* have been demonstrated in the blood. Thus according to Michaëlis and Cohnstein, there is an enzyme which in the presence of red blood corpuscles and oxygen destroys fat (lipolytic enzyme). Arthus has found an enzyme which splits monobutyrin into glycerin and butyric acid; but an enzyme which would split neutral fat has not been certainly demonstrated. Further, a diastatic enzyme which changes starch into maltose, one changing the latter into dextrose, and an enzyme by which sugar is destroyed (glycolytic enzyme), are said to be present. Hedin mentions a feeble enzyme which digests proteid in an alkaline medium.

Likewise there are found in the blood substances which act against the enzymes peculiar to the body, represent therefore *antienzymes*, and develop antipeptic, antitryptic, and antichymotic effects.

Serum contains moreover certain substances which have the power to kill Bacteria and foreign cells generally. The serum of one animal species destroys the blood corpuscles of another species, if the species are not very closely related—a fact which explains, in part at least, the harmful effects of a transfusion of foreign blood. This globulicidal action, as it is called, as well as bactericidal action of the blood is very different in different genera of animals. Thus the serum of horse's blood is only slightly poisonous to man and is tolerated in pretty large doses. The serum of human blood exercises a powerful effect on the typhoid and cholera bacteria, while on the pus-forming staphylococci a weaker effect, and on the streptococci, the diphtheria and anthrax bacilli, no effect at all. On the other hand the serum of the rabbit kills the bacteria of anthrax and of typhoid fever, but is harmless for the pus-forming staphylococci, etc.

It has long been known *that many diseases confer on the individual who survives them, as an after effect, an immunity or unsusceptibility toward those particular diseases.* Now it has been shown (Behring and Kitasato, 1890) that the blood or the serum of an individual who has become immune in this way against an infectious disease, has the property, when it is injected in sufficient quantity, of conveying the immunity to another individual previously susceptible to the disease. A blood or serum of an individual who has successfully withstood the disease receives therefore as an after effect properties which it did not possess before.

These discoveries represent the point of departure of numerous investigations on the various *changes which appear in the blood after injection of different substances.* In general, one may say that if a foreign substance of a certain kind (such as the toxins formed by the Bacteria, foreign blood, various proteid substances, finely minced organs, etc.) is brought into the animal by subcutaneous, intraperitoneal or intravenous injection, the blood of the animal acquires the ability to change the foreign substance in some way, and thus to neutralize its effect on the organism. Since in such cases there are found in the blood specific *antibodies*, we infer that the changes appearing in the blood are of different kinds according to the nature of the substance injected.

If a bacterial toxin is injected into the blood, there arises in the latter an *antitoxin* specific for just this toxin, which has the power to abolish the effect of the former, probably by a kind of neutralization. Different toxins possess an elective power for different cells of the body; and precisely those cells which are attacked by a definite toxin appear to be most active in the formation of the antitoxin. By a kind of internal secretion the antitoxin is given off to the blood and in such abundance that it may be used (for example, diphtheria serum) as a remedy in other animals.

The power of the blood to *destroy blood corpuscles, Bacteria and foreign cells generally*, like its antitoxic properties, can be increased by the addition of appropriate substances. Here also we have to suppose that under the influence of the foreign cells, the cells of the body (certain leucocytes especially) are the seat of production of the antibodies. As with the antitoxin serum, the *cytolytic* serum can also exercise its specific effects outside of the body—from which it follows that these are not bound up in the formed constituents of the blood, and in general not in the living substance.

If the serum of an animal immunized against—say typhoid fever—is mixed with a fluid culture of *Bacillus typhosus*, the latter become stuck together, *agglutinated.* There has been formed in the blood of the animal therefore a substance which produces this effect. The same influence may be observed also on the blood corpuscles. When an animal has been treated with a foreign blood, its own serum added to the blood in question brings about an entirely similar agglutination of the corpuscles of the foreign blood.

After intraperitoneal injection of cow's milk the serum of the animal employed acquires the ability to throw down a precipitate in the cow's milk—i. e., a *precipitin* has been formed in the blood. By injection of different kinds of blood or proteid solutions, one may obtain different *precipitins* which on the whole are specific since they produce precipitates especially well in solutions of the substances injected. This specific character is not however by any means absolute.

If we add to what has been said above, that after the injection of an agglutinating serum into an animal an *antiagglutinating* effect may be obtained, after injection of a precipitating serum an *antiprecipitating* effect, after a cytolytic serum an *antilytic* effect, it ought to be apparent without further discussion that under the influence of various chemical agents, extraordinarily important and complex changes can be induced in the blood.

These changes are produced in part by a special activity of different cells of the body, developed by the attack, in part by certain leucocytes.

There can be no doubt that all these changes are *protective adaptations of the body against harmful influences.* Especially is this true of the antitoxins, the bacterialysins, and agglutinins.

The matter is not so clear with regard to the other lysins and the precipitins; but it is to be presumed that they also have some definite purpose. It appears that they are specialized substances, which, like the antienzymes, come down in the globulin precipitates; but whether they are true proteid bodies or are only attached to such, cannot be said definitely as yet.

We must forego a presentation of the theoretical views which are held in explanation of these phenomena, since a discussion of them would require too much space. We would not, however, omit to mention the *side-chain theory* of Ehrlich, since this has had a very stimulating effect on research in this field, and has very successfully gathered together under one general point of view the complicated phenomena which confront us in this province.

Since the chemical processes in different organs are in many respects very different, the blood returning by the vein must have a more or less *variable constitution according to the organ from which it flows.* Analysis of these different kinds of blood would be well calculated to give at some future time very valuable conclusions as to the chemical transformations taking place in the corresponding organs. At present however our information is quite too inadequate for any discussion of the subject.

The blood flowing from the different parts of the body is collected finally in the two venæ cavæ and is emptied by them into the right heart, where the different kinds of blood, not yet thoroughly mixed in the veins, are mixed together; *so that blood driven from the left ventricle to all parts of the body is entirely homogeneous.*

B. COAGULATION OF BLOOD

If blood be drawn directly from an open artery into a saturated solution of magnesium sulphate, it can be kept for days without coagulating. The blood corpuscles can be removed from such blood by filtering, by centrifugalizing, or simply by letting it stand, and in this way a fluid is obtained known as the *salt plasma* (Alex. Schmidt). By precipitation with an equal volume of saturated NaCl solution, there is thrown down a proteid body, the *fibrinogen,* which can be further purified by various means. Fibrinogen is soluble in weak NaCl solution and its solution will keep at room temperature until putrefaction sets in without showing a trace of coagulation. *If however some blood or blood serum be added to such a solution, fibrin formation takes place* *at once.* The same effect is produced also by blood clot washed free of all color with water. Such a clot contains fibrin and the remains of white corpuscles, so that one is inclined for many reasons to assume that the substance which must be added to a solution of fibrinogen to make it clot, and which has been designated the *fibrin ferment* or *thrombin* (A. Schmidt) comes directly from the white blood corpuscles. It appears from several observations that the white corpuscles themselves do not of necessity break down under such circumstances, and Arthus has expressed the view that they give off the fibrin ferment by a process of secretion.

Coagulation cannot take place, as Arthus was the first to demonstrate, *without the presence of a soluble calcium salt.* This is probably due to the fact that fibrin ferment does not exist in the blood as such but in the form of a mother substance, or zymogen, and is activated only in the presence of Ca salts (Hammarsten, Pekelharing). The calcium does not appear to be necessary for the formation of fibrin, however, for a solution of fibrinogen coagulates in the presence of thrombin even when the calcium salts are removed by an oxalate.

Coagulation is considerably accelerated *by addition of extracts of all possible kinds of organs,* and even by mere contact of the blood with the wound. On this account it has been assumed that the contained nucleo-proteids might represent precursors of the thrombin. On the contrary Arthus, Morawitz and others believe that they only hasten the formation of the enzyme and that the mother substance of the latter occurs exclusively in the blood.

According to Morawitz the organ extracts effect the formation of the proenzyme from a zymogen stage, *thrombogen,* whereupon thrombin arises from the proenzyme under the influence of the calcium ions.

The formation of thrombin is stopped immediately by sodium fluoride and by addition of this salt in small quantities it is possible therefore to follow the course of thrombin formation more closely. In this way it has been shown that at the moment it flows from the vessel the blood contains no thrombin at all, that the quantity of the enzyme increases quite slowly at first, and that shortly before coagulation it undergoes a rapid increase. Thrombin is formed for a time also after coagulation has taken place (Arthus).

When blood serum stands exposed to the air its enzyme gradually decreases in quantity and disappears entirely after about six days. No more enzyme is obtained after this time by addition of calcium salts. But by means of acids, alkalies, alcohol, etc., one can demonstrate an effective fibrin ferment; there is present therefore in the serum a body from which active fibrin ferment may be formed. This body is absent from normal plasma and seems to make its appearance for the first during coagulation. According to Fuld and Morawitz, it is probable that this substance is thrombin itself, which had merely passed over to an inactive state.

The transformations brought about by enzymes in general appear to proceed in such a way that the substance acted on absorbs water and is subsequently split into two new substances. This is probably the case in fibrin formation; the fibrinogen is split into insoluble fibrin which constitutes the chief bulk, and *fibrino-globulin* which remains in solution and is formed only in small quantity (Hammarsten).

The difficulties with which the subject of coagulation is beset, and which we have been able to discuss here only in a cursory manner, are still more multiplied when we ask *why the blood does not clot in the vessels.* That the constant movement of the blood is not the reason is proved by the fact that blood coagulates outside the body more rapidly when it is stirred. Cooling of the blood cannot account for coagulation, for it is possible to postpone the process for a long time by this very means. Neither can contact with the air be considered, for coagulation goes on in the usual manner if blood is collected (over mercury) by exclusion of air.

Coagulation does not occur if the blood is drawn by means of an oiled cannula, or if it is caught in an oiled vessel: in fact it can now be stirred with an oiled rod without producing coagulation. But if it is stirred with an ordinary rod, or if small solid particles be introduced, coagulation takes place immediately (Freund). The reason why coagulation does not take place under the above-mentioned circumstances doubtless lies in the fact that the blood is prevented by the oil from coming in contact with the wall of the vessel. Attempts have been made to explain the absence of coagulation in the blood vessels in a similar manner, by assuming that in health the necessary adhesion of the blood to the walls is wanting. When the endothelial lining of the vessels becomes abnormally changed in any way so that internal adhesion occurs, intravascular clotting ensues. Against this conception however it may be objected that the blood always thoroughly wets the internal wall of the blood vessels (B. Lewy).

Beautiful examples of the inhibiting property of the vascular walls are found in the facts that blood remains fluid for a long time in a section of a vein ligated off at both ends (Hewson): and that a turtle's heart filled with blood beats for days without any clotting if the temperature of the contained blood be low (Brücke).

Opinions differ considerably as to the real nature of the changes produced by adhesion of the blood to rough surfaces, so that at this time we are unable to form any definite conception of the matter. But since substances have been found in the blood which exercise an inhibiting influence on coagulation, it is at least conceivable that during life and with uninjured vascular walls, the inducing and inhibiting bodies neutralize each other, while in shed blood the former preponderate and thus bring about coagulation.

In the living body the coagulability of the blood can be abolished by intravascular injection of *albumoses* (Schmidt-Mühlheim, Fano) or of *leech extracts* (Haycraft). If the blood is diverted from the liver and the intestine so that it circulates only through the extremities, the head and the lungs, it likewise loses its ability to coagulate.

Coagulation of the blood is of extremely great importance *as a means of protection* for the body, since bleeding from injured vessels, unless they be too large, is thereby stopped. If the blood did not coagulate every slight injury would involve great loss of blood. When the larger vessels are ruptured coagulation does not suffice: for the blood flows out in such quantity and with such speed that the first blood does not have time to coagulate before new blood replaces it. And if coagulation should take place in the wound, the clot would not be sufficiently firm to withstand the great force of the escaping blood.

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CHAPTER VI

CIRCULATION OF THE BLOOD

If the blood were to stand still in any particular vascular region, it would become impoverished in nutrient substances, especially oxygen, would become overladen with products of tissue activity, and so would be rendered unfit to fulfill its physiological purposes. But by the fact that *the blood is continually in motion,* this is prevented, for as it moves it both replenishes its store of nutrient substances taken from different parts of the body and gets rid of the products which are useless or harmful to the body.

This continual movement is maintained by the *activity of the heart.* The heart represents the motive power which drives the blood through the vessels. The latter however are not mere passive tubes, but in various ways they *actively participate* in the distribution of the blood throughout the body.

FIRST SECTION

GENERAL SURVEY OF THE BLOOD'S MOVEMENTS

The heart of warm-blooded animals is divided by means of a septum running from above downward, *into two completely separated halves, a right and a left* (Vesalius, 1542). Each half consists of two communicating chambers, an upper, *the auricle*, and a lower, *the ventricle.* The opening between auricle and ventricle can be closed in both halves of the heart by means of valves.

Blood vessels connect with both auricles and ventricles. In those leading from the ventricles blood flows *from* the heart, and they are called *arteries.* In the vessels communicating with the auricles blood is conveyed *to* the heart, and they are called *veins.*

The arteries communicate with the veins by means of the *capillaries,* so that the heart and the vessels form a connected system of tubes entirely shut off from the outside.

In this system, as was first established by Harvey (1628), the blood moves in the following manner (Fig. 50). It is poured by the two venæ cavæ into the *right auricle,* and is driven by the *latter* into the right ventricle. By the contraction of the ventricle it is pressed out into the *pulmonary arteries* proceeding therefrom, and flows through the vessels of the lungs and the pulmonary veins into the left auricle. This part of the circulation is called the *lesser circulation,* and was first described by Servet (1553) and Colombo (1559). From the left auricle the blood is driven into the *left ventricle* and from there again into the *aorta*. Thence it flows through all branches of the aorta to the capillaries, from there to the systemic veins and through the *venæ cavæ* back to the right auricle. That portion of the circulation from the left ventricle to the right auricle is called the *greater circulation*.

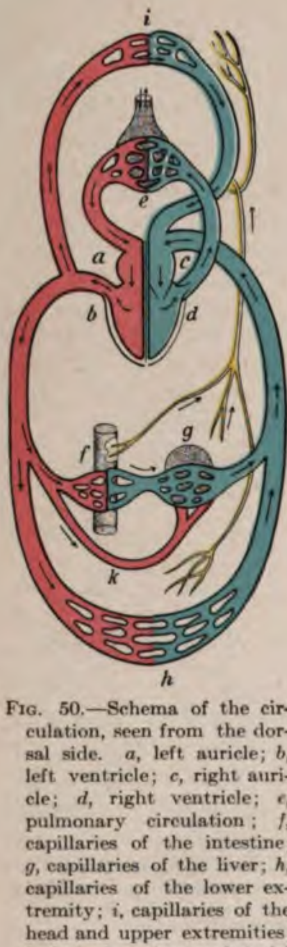

Fig. 50.—Schema of the circulation, seen from the dorsal side. *a*, left auricle; *b*, left ventricle; *c*, right auricle; *d*, right ventricle; *e*, pulmonary circulation; *f*, capillaries of the intestine; *g*, capillaries of the liver; *h*, capillaries of the lower extremity; *i*, capillaries of the head and upper extremities; *k*, hepatic artery. Arterial blood, red; venous blood, blue; lymph vessels shown only in outline.

In warm-blooded animals the entire quantity of the blood must flow through the lungs in order to pass from the right half of the heart to the left. During a complete circuit therefore the blood flows through two systems of capillaries: namely, (1) that of the greater circulation, and (2) the pulmonary system. For the blood which passes through the *capillaries of the stomach, intestine, pancreas and spleen* still another capillary system is interpolated. This blood flows to the liver in the portal vein which there breaks up into a new system of capillaries, whence arise the hepatic veins, conducting the blood away to the heart. The same is true of the kidney blood, for in the kidneys themselves the blood flows first through the capillaries which form the glomeruli of the Malpighian corpuscles, and secondly through the capillary plexus by which the kidney tubules are surrounded.

The contraction of the heart is designated the *systole* and its relaxation, the *diastole*.

SECOND SECTION

THE MOVEMENTS OF THE HEART

§ 1. THE FORM CHANGES OF THE HEART IN SYSTOLE

After opening the pericardium of a beating heart it can be seen that the contraction begins at the outlet of the great veins, which are here surrounded by circular muscle fibers, and proceeds thence onto the auricles.

The two auricles *contract simultaneously*, and immediately after the auricular systole the ventricles contract, *likewise simultaneously*. Neither auricles nor ventricles completely empty themselves by their contractions.

A. STRUCTURE OF THE VENTRICULAR WALL

The arrangement of the muscular mass which forms the walls of the ventricles is very complicated. Our description here must be very brief.

Of the two ventricles the left possesses a much stronger musculature than the right, a condition which conforms with the much heavier work to be done by the former. In fact the outer wall of the right ventricle is formed for the most part of fibers which come from the left. To a certain extent therefore the right ventricle may be looked upon as a cleft in the wall of the left, as shown in Fig. 51.

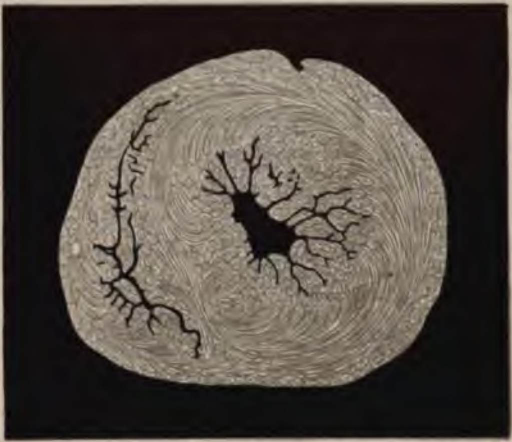

FIG. 51.—Cross-section through a fully contracted human heart at the junction of the upper and middle thirds, after Krehl.

With regard to the structure of the ventricles the following is worthy of mention: From the fibro-tendinous rings at the base of the left ventricle, and from the muscular sides of the aorta superficial fibers pass obliquely downward to the apex of the heart, enter for the most part the vertex of the left ventricle and double round into its interior, to be inserted either into the papillary muscles and chordæ tendineæ, or into the atrio-ventricular ring. The two layers thus formed are separated by a median layer, which, when isolated by a special method of preparation, has the form of a muscular cone. It is connected also by many fibers with the outer and inner layers. The fibers of this median part describe loops, which, not having any tendinous connections, return to their starting point (Fig. 52). It is obvious that this strongly developed median layer must play a prominent part in the contraction of the left ventricle.

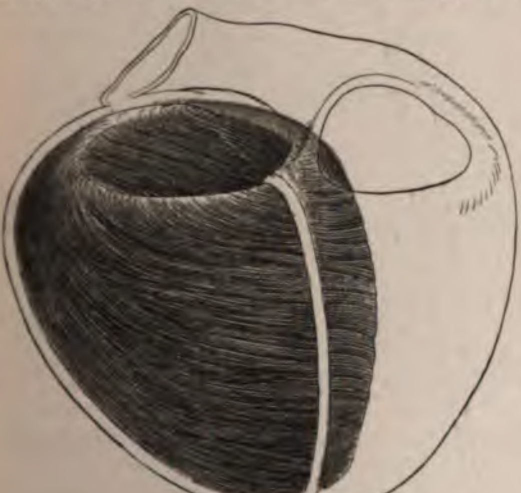

FIG. 52.—Layer of fibers in the left ventricle of the human heart which have no tendinous insertions. The more external and more internal layers have been removed. The outline of the entire heart is shown. After Krehl.

The synchronism of contraction of the two ventricles naturally depends on the fact that the muscular fibers are in part common to both ventricles. Nevertheless various observations indicate that *this synchronism is not an absolute one, but that each ventricle possesses a certain physiological independence* (Knoll).

B. THE FORM CHANGES OF THE HEART

In diastole the form of the ventricles of an empty heart outside the body depends in the main upon the way in which they are supported, whereas under normal circumstances their form depends in the main upon the degree to which they are filled. In systole when, as Harvey put it, " the heart makes tense all of its fibers," the ventricles whether empty or filled have a perfectly definite form, which is entirely independent of the diastolic form. Hence if the heart is lengthened in any one of its diameters during diastole, it is shortened in this diameter during systole.

In the living body and in the unopened chest the heart lies in the pericardium and is covered for the most part by the lungs. It is suspended upon the great arteries and so far as the pericardium will permit, is movable in different directions.

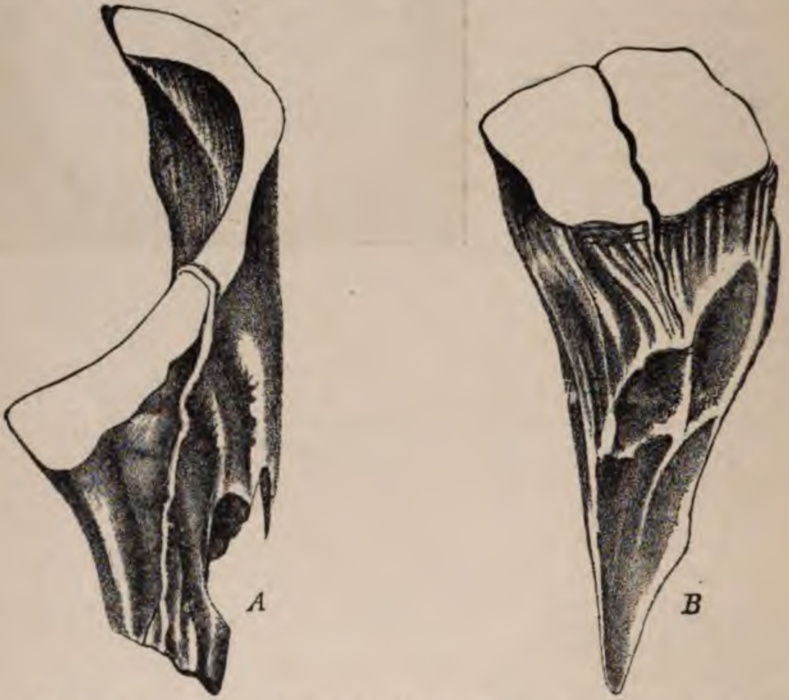

FIG. 53 —Casts of the ventricular cavities of the ox heart in rigor mortis, after Worm-Müller and Sandborg. *A*, cavity of the right ventricle; *B*, of the left. Two-thirds natural size.

If one observes the heart of a mammal in the usual supine position of the animal in experimentation, the diastolic heart is flattened somewhat in the anterior-posterior direction, while its transverse diameter is increased. Under such circumstances one finds that the long axis and the transverse diameter shorten in systole, while the sagittal axis becomes longer.

In the natural position of the body the heart is supported for the most part by the lungs; these are to be looked upon as air cushions which influence the form of the diastolic heart only to a slight extent. In the natural position of the animal therefore the base of the heart must be more circular than in the supine position with the chest open. By means of needles stuck through the chest wall into different parts of the heart, so that their ends gave by their movements the directions of shortening, Haycraft found that the heart in its natural position contracts in all its dimensions.

According to Braun, in the shortening of the long axis of the heart during systole its conical end becomes blunter and the long axis of the left ventricle comes to form with that of the right a more acute angle than during diastole; at the same time the apex of the heart moves slightly to the right.

Since the apex of the heart is its freest part, one would suppose that on contraction of the long axis in ventricular systole the apex would approach the base. But this is not the case: the base on the contrary approaches the apex, and the heart as a whole makes no change in position. This phenomenon appears to be explained partly at least by the recoil of the blood when it rushes out through the arterial openings. That is to say, when the ventricles drive the blood into the great arteries the apex is prevented by this recoil from moving toward the base; and instead, presents a relatively fixed point toward which the base is drawn (Chauveau and Faivre).

The changes in form of the heart cavities have been studied only in heat or in death rigor, where the contraction of the heart muscle has proceeded much farther than it ever does in life. From such observations it appears that even in these extremely contracted conditions the *cavities of the heart are never entirely obliterated.* In the left ventricle an evident cavity remains above the summits of the papillary muscles; while the right ventricle is transformed into a narrow slit, so that the two walls in the upper portion underneath the atrio-ventricular opening are still separated from each other by a certain distance (Hesse, Worm-Müller and Sandborg; cf. Fig. 53).

§ 2. THE REGULATION OF THE BLOOD FLOW THROUGH THE HEART

The normal course of the blood through the heart is determined *chiefly by its valves,* but partly also by other means, which prevent the blood from flowing in the wrong direction.

A. THE ATRIO-VENTRICULAR VALVES

Between the auricle and ventricle we have in the right heart the *tricuspid valve,* in the left the *mitral valve.*

The tricupsid is composed of a tubular membrane fastened around the entire circumference to the atrio-ventricular ring. It is divided by deep incisions into *three large and one or two small flaps.* These are attached by means of the chordæ tendinæ to the papillary muscles or to the ventricular wall. The chordæ tendinæ run partly to the free edge of the valvular flaps, partly to their ventricular surface where they are attached broadly to the connective-tissue framework of the flaps.

The *mitral valve* is similar in all essential respects to the tricuspid, only it is more firmly constructed in all its parts and consists of but *two flaps.*

When the ventricles contract the blood is prevented by closure of the valves from flowing back into the auricles, and is forced to take the right path into the arteries. Without the valves not a drop of blood would reach the arteries, for the resistance in the arteries is considerably greater than that in the auricles and in the great veins emptying into them.

During the ventricular diastole the atrio-ventricular flaps are more or less closely approximated by simply floating into position on the blood as it fills the ventricle. When the ventricular systole sets in and the pressure in the ventricles rises suddenly, the valvular flaps naturally strike together and so cut off connection of the ventricle with the auricle.

Because the pressure in the auricle at the systole of the ventricle is infinitesimally small as compared with that in the ventricle itself, the valves must close so quickly that at most only a very insignificant quantity of blood can get back into the auricles before the closure is complete. It appears even that the valves work so promptly that *absolutely no regurgitation of the blood* into the auricle takes place. When the auricle contracts, the ventricle is somewhat distended owing to the flexibility of its resting wall and its contents are subjected to a certain tension. At the moment the contraction of the auricle abates somewhat or ceases altogether the pressure in the ventricle becomes greater than that in the auricle, and by this means the valvular flaps are brought together even before the ventricular systole begins (Baumgarten).

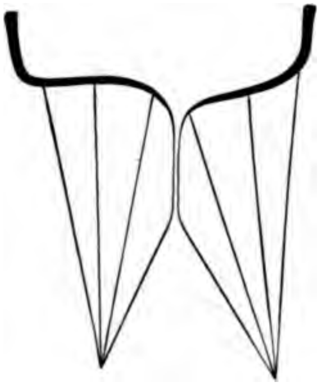

FIG. 54.—Position of the atrio-ventricular valves when closed, schematic drawing, after Krehl.

The great pressure which is brought to bear on the valves during the ventricular systole would cause them to turn up into the auricles, and thereby cause serious disturbance to the circulation, were it not for the chordæ tendineæ. Since the chordæ are attached not only at the free edges but also on the flat surface of the valves, the latter are prevented not only from turning up into the auricle, but even from bulging toward it.

Because of the chordæ tendineæ the closed valve takes a perfectly definite position, the central parts of the flaps being pushed up to the level of their attachment, and their turned-down edges being applied to each other as in Fig. 54. By this means closure is established over a greater surface and is secured also by the fact that the bent portions of the edges dovetail into each other by toothlike folds, so that the valves are able to sustain the great pressure. The circumference of the base of the heart, and at the same time that of the atrio-ventricular opening, becomes very much smaller in ventricular systole: the muscles surrounding the opening therefore must be credited with a share in the closure of the passage.

The rôle of the *papillary muscles* in the closing of the atrio-ventricular valves has been conceived in very different ways. The most probable view is, that they prevent swinging of the valves into the auricles, the approach of the heart base toward the apex being compensated by their contraction and consequent pull on the chordæ tendineæ.

When the auricles contract, regurgitation of blood into the great veins is prevented by contraction of the circular musculature passing around the latter, their openings being in this way either narrowed considerably or actually closed.

B. THE SEMILUNAR VALVES

Since the blood cannot flow back into the auricle during the ventricular systole, it must pass into the great arteries. The mouths of the latter are closed by means of valves, each consisting of *three pouchlike flaps.*

These flaps are semicircular membranes, fastened by their curved edges to the wall of the vessel, so that they stand out with their straight edges from the wall and present concave surfaces toward the arteries. In this way pouches are formed in which the blood is caught and dammed back, while at the same time the wall of the pocket turned toward the lumen of the vessel is put on the stretch.

In both the aorta and the pulmonary artery the wall bulges outward directly above the attached edges of the valve, forming in each three enlargements, the *sinuses of Valsalva.* In the aorta one sinus is directed backward, two forward, right and left. From the latter two the *right* and *left coronary arteries* take their origin.

When the pressure in the ventricle is lower than in the corresponding artery, the semilunar valves are closed with their edges applied tightly together. When the pressure in ventricular systole increases enough to exceed that in the aorta or pulmonary artery, the valves open and the blood flows out. When the ventricle again passes into diastole the valve is closed once more.

What position the valves take in systole is not yet definitely determined, although various observations make it probable that their free edges stand out some distance from the sinuses, thus narrowing the arterial mouths. It should be added that there are certain muscular folds springing from almost all sides of the artery, which serve as supports for the valves (Krehl).

In consequence of this arrangement the blood is pressed through a narrow muscular cleft into a wider space above the valves. This must cause vortices and eddies to be formed, which tend constantly to press the flaps of the valve together, and they are unable so to do only because the blood is being forced through at high pressure. When the outflow ceases, the valves are pressed together suddenly, *and without any regurgitation.* The closure is rigidly maintained by the difference between aortic and ventricular pressures, a difference which is more than sufficient once the muscles of the ventricle relax and the above-mentioned muscular supports of the valves give way.

§ 3. THE HEART SOUNDS

If the ear be placed over the breast wall, with every heart beat one hears a *dull, long-drawn-out sound,* and after this *a shorter, clear sound.* Then follows a pause, then again the dull sound, and so on. The long sound is called the first heart sound, the following one, the second. The first is heard throughout the entire ventricular systole, and only then. The second follows immediately after the first, i. e., immediately after the end of the ventricular systole, and after it comes the pause.

The cause of the first heart sound is to be sought chiefly in the *so-called muscle tone*; that is to say, in the tone or noise which is to be heard whenever a muscle contracts (cf. Chapter XV). The first sound is clearly audible in the case of a heart which is almost entirely empty of blood and air, and in which accordingly the valves cannot be stretched and cannot therefore be set in vibration (Ludwig and Dogiel).

Other factors coöperate in the production of the first sound, notably the *closure of the atrio-ventricular valves* at the beginning of systole, and the vibrations set up in them and in the blood by their closure. It is not impossible that vibrations which are caused by the opening of the semilunar valves play a certain part also in the production of this sound. However the most prominent factor of all is a muscle sound with which these other sounds are associated.

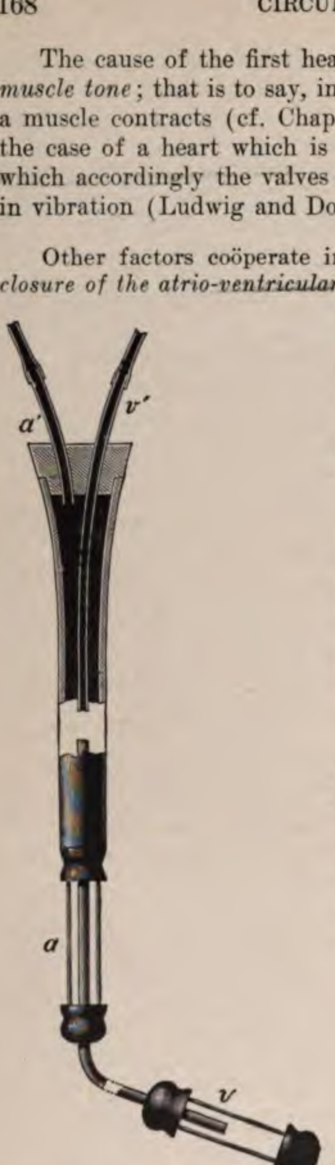

Fig. 55.—Heart sound, after Chauveau and Marey.

The second heart sound is produced by the *sudden tension of the semilunar valves*, and by other simultaneous vibrations in the blood consequent upon their closure. Sudden stretching of these valves in an excised aorta produces a sound which agrees exactly in character with the second heart sound (Carswell and Rouanet).

It will be apparent at once that we have in reality four sounds, two first and two second. Practical experience teaches however that the first two occur simultaneously and the second two simultaneously: and this is also evidence of the fact that both ventricles begin their contractions simultaneously and that the semilunar valves of the two sides are closed at the same instant.

§ 4. PRESSURE CHANGES IN THE HEART DURING ITS ACTIVITY

A. TECHNIQUE

In order to measure the pressure and its variations in different chambers of the heart, it is necessary that these should be connected with a manometer. This can be done in the closed thorax by passing a cannula or sound from the carotid through the aorta into the left ventricle, in which one must so far as possible avoid injury to the semilunar valves (Chauveau and Marey). Sounds can be passed likewise by the jugular vein into the right auricle and right ventricle. In the opened thorax sounds can be thrust either directly through the walls into the different heart cavities, or they can be passed into the ventricles first through the walls of the auricles, then through the atrio-ventricular openings.

Various instruments have been constructed for the study of the pressure variations. The requirements for such an instrument are very severe: indeed there occur in the ventricles variations of 130 mm. of Hg. in 0.06 of a second —i. e., 2,170 mm. Hg. in a second. The instrument to be used must be capable therefore of righting itself very quickly, and must be at the same time to a high degree aperiodic so that it has no oscillations of its own. The first instrument used for this purpose was the writing tambour of Marey. This was connected with a sound of peculiar construction (cardiographic sound) passed into the heart chambers. Such a sound (Fig. 55) consists of a tube, the end of which, to be placed in the heart chamber, carries a rubber bulb. The latter is supported by a steel frame (*a*, *v*) so that it is not completely compressible. The free end of the sound is connected with the writing tambour. With the pressure changes in the heart cavity the air pressure in the bulb changes and the writing tambour records these variations graphically. By suitable means the curves thus obtained can be estimated in absolute terms (millimeters of Hg.).

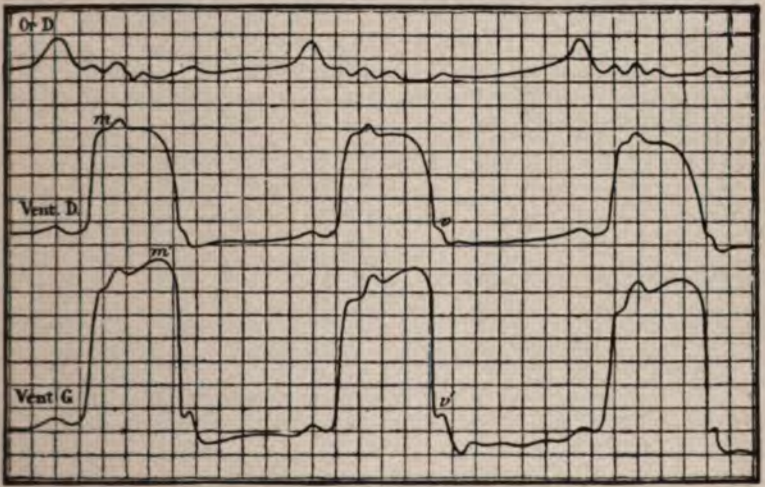

FIG. 56.—Intracardial pressure curves of the horse, after Chauveau and Marey. Or. D., right auricle; Vent. D., right ventricle; Vent. G., left ventricle.

B. PRESSURE VARIATIONS IN DIFFERENT CHAMBERS OF THE HEART

As already observed the auricles contract first. The duration of their systole up to the point of maximum pressure is, in the horse, 0.1 second: that of the ventricles up to the point where the fall in pressure begins is considerably longer, namely, 0.4 second (also in the horse). The maximum pressure in the right auricle of the dog is given as 20–22 mm. Hg. (Goltz and Gaule).

The form of the pressure variations in the heart chambers is variously figured, according to the instruments used in their graphic registration. The difference is due to the fact that not all the different instruments give the rapid variations in pressure with sufficient exactness.

The most correct form of the intracardial pressure curve appears to correspond to the type represented in Fig. 56. If we neglect details which are relatively unimportant, the intracardial pressure runs somewhat as follows:

(1) *a small elevation,* (2) *a very steep ascent,* (3) *a subsequent much slower ascent, or a plateau almost parallel to the abscissa,* (4) *a rapid fall from the maximum,* (5) *a very gradual ascent* (Fig. 56).

The maximum pressure of the ventricular systole has been determined also by the Hg-manometer, by interpolating between the heart and the Hg a maximum valve which opens with every increase in the ventricular pressure, but prevents the return of mercury with the fall of pressure.

The *maximum pressure* in the left ventricle may amount to 200 mm. Hg. (in the dog). The pressure in the right ventricle is considerably lower; in the dog the pressure in the pulmonary arteries varies between 10 and 33 mm. Hg., in the rabbit between 6 and 35, and in the cat between 8 and 25 mm. Hg. A definite ratio between the pressures in the lesser and the greater circulations does not obtain, because even with very great variations in pressure in the greater circulation, only relatively slight variations generally occur in the lesser (cf. Section III, § 8).

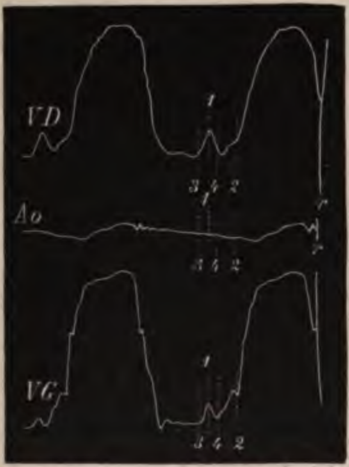

Fig. 57.—Pressure curves of the right ventricle (*V D*), of the left ventricle (*V G*), and of the aorta (*A o*) of the horse, after Chauveau. 3–4 auricular contraction; 4–2 intersystole. To be read from left to right.

On the pressure curves given above, various single points are found which are sometimes more, sometimes less clearly marked. Some of these—e. g., various peaks which occur in many tracings at the height of the plateau—are doubtless artifacts produced by extreme vibrations, while others are definite expressions of events in the heart. The latter we must discuss, therefore, somewhat more in detail.

At the beginning of the pressure curve, before the ascent which corresponds to the strong rise in the ventricular systolic pressure, a slight elevation is sometimes very beautifully shown. This elevation, as we learn from Fig. 56, is caused by the *auricular contraction* and the consequent rise in pressure in the ventricle.

In the intracardial pressure curve of the horse, Chauveau has demonstrated between the peaks corresponding to the auricular systole and the beginning of the true ventricular systole a more or less clearly marked *intersystole* (Fig. 57). A similar elevation appears now and then also in the cardiagram of man, and represents doubtless a brief rise in the pressure inside the ventricle. This has been referred with great probability to the elastic rebound of the ventricular wall after the completed auricular systole. Obviously it can appear clearly only in case a measurable time intervenes between the maximum of the auricular contraction and the beginning of the ventricular systole.

After the ventricular systole has begun, it requires a certain time before the power of contraction becomes sufficient to overcome the pressure exerted by the blood in the vessels upon the semilunar valves (*period of rising ten-*

sion). It is evident that the *semilunar valves must open the moment the pressure in the aorta is exceeded* by that in the ventricle. So smoothly is this point passed that it is not marked on the pressure curve by any special fluctuation.

The *period of rising tension* can be determined on an animal by recording the pressure in the aorta and in the left ventricle at the same time. It is found (cf. Fig. 58) that the pressure curve of the ventricle rises from the abscissa in the horse about 0.1 second, in the dog 0.03 second earlier than does the pressure curve of the aorta. The period shows but slight variation with varying blood pressure or with different rates of heart beat, which means that the heart possesses in a very high degree the ability to meet almost without loss of time very different demands upon its powers.

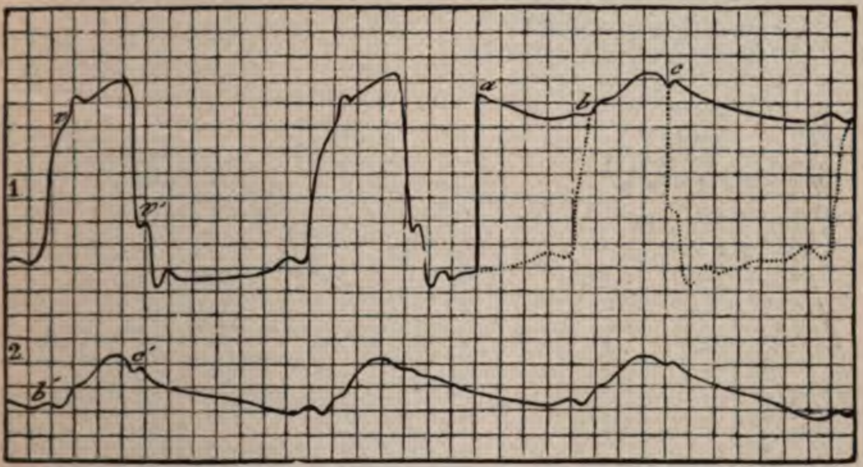

FIG. 58.—Pressure curves from the left ventricle (1) and the aorta (2), of the horse, after Chauveau and Marey.

In man the period of rising tension has been obtained by comparison of the simultaneous apex and pulse curves, and is given by different authors at from 0.05 to 0.1 second.

Closure of the semilunar valves must take place whenever the pressure in the aorta exceeds by ever so little that in the left ventricle. By simultaneous registration of pressure in the aorta and in the left ventricle it has been found that the moment of equal pressure follows shortly after the beginning of the steep descent in the ventricle, but this instant is not shown in any special manner on the tracing.

So long as the pressure in the ventricle is higher than that in the aorta or pulmonary arteries, the blood is being driven out of the heart. The duration of the *period of ejection* depends on the aortic pressure at the beginning of systole, or upon the pulse frequency only to a very slight extent: it amounts to about 0.18–0.20 second in the dog.

At the close of systole the heart chambers gradually fill with blood and as a consequence the intracardial pressure gradually rises slightly.

§ 5. THE APEX BEAT

We have in the apex beat a means of studying the different questions which have to do with the pressure relations and the form changes of the heart in the normal animal and in man. By placing the hand on the chest wall, where the heart is not covered by the lungs—i. e., in the fourth or fifth intercostal space—an impulse can be felt with every ventricular systole, which is called *the apex beat.* In lean individuals an elevation of the intercostal wall can be observed with the eye. This fact is of itself sufficient to show that the heart actually strikes against the chest wall, but does not on the other hand prove that the ventricle withdraws from it in diastole. In diastole the heart is flabby and weak. If one presses with the finger on the exposed heart at this time, only a little resistance is felt, even though the finger does not make a permanent impression.

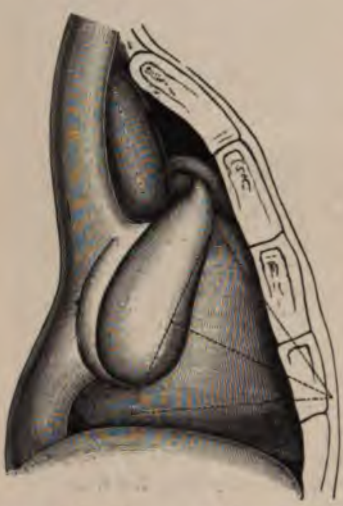

FIG. 59.—Schema illustrating Ludwig's theory of the apex beat. The dotted line represents the position of the heart in systole.

As soon however as the ventricular systole begins, the heart suddenly becomes hard and exerts a very strong pressure on the finger. Everywhere it feels as if the finger were being pressed against. *This sudden hardening is the essential cause of the apex beat* (Harvey, Kiwisch, Marey). In addition to this however there is an effort on the part of the ventricle to assume such a form that the apex will stand vertical to the base (Carlile, Ludwig). Consequently the heart in its systole takes the position with reference to the chest wall described by the dotted line in Fig. 59. The apex, therefore, strikes against the thoracic wall and pushes it forward to a slight extent.

In opposition to this, Shreiber remarks that the heart chambers must assume the same form (a right cone) after the auricular contraction and before the beginning of the systole. But this follows of necessity only in case the ventricles become turgid with blood—a thing which rarely results from auricular contraction. With an ordinary filling of the ventricles their diastolic form may be very different, just as an india-rubber balloon may vary in shape until it is highly inflated, when it becomes spherical.

Other factors also have been brought forward for theoretical explanation of the apex beat. It has been assumed, for example, that the heart beat against the thoracic wall is due chiefly to the rebound consequent upon the ejection of blood from the ventricle, or in other words, has its origin in the stretching and elongation of the great arteries by means of which the heart is thrown forward. It is possible that these factors do in fact contribute to a certain extent in producing the beat. But that they are not the only factors, and do not even represent the most important mechanism concerned, appears from such facts as these: first, the forward movement can be observed on an excised heart empty of blood as well as on one with ligated arteries; and secondly, the movement appears immediately at the beginning of the ventricular systole, while the opening of the semilunar valves and the ejection of blood into the great arteries follows appreciably later (cf. page 171).

The apex beat offers the only possibility of studying the heart movements on a living man, and for this reason much attention has been devoted to its graphic record, called the *cardiogram*.

On animals the intracardial curve and the cardiogram can of course be recorded simultaneously, the latter by pushing in between the chest wall and the heart a small balloon which communicates with the writing tambour. In the two curves, as shown in Fig. 60, we observe various similarities and differences. In both we have at A the elevation caused by the auricular contraction; likewise the steep rise at the beginning of the systole. On the cardiogram this reaches its maximum earlier than does the ascending limb of the pressure curve (B). After the maximum is once reached the pressure curve runs almost parallel with the abscissa, or it rises gradually, then sinks suddenly at the end of the ventricular systole. The cardiogram begins to fall much earlier, but does so more gradually although finally it shows also a steep fall.

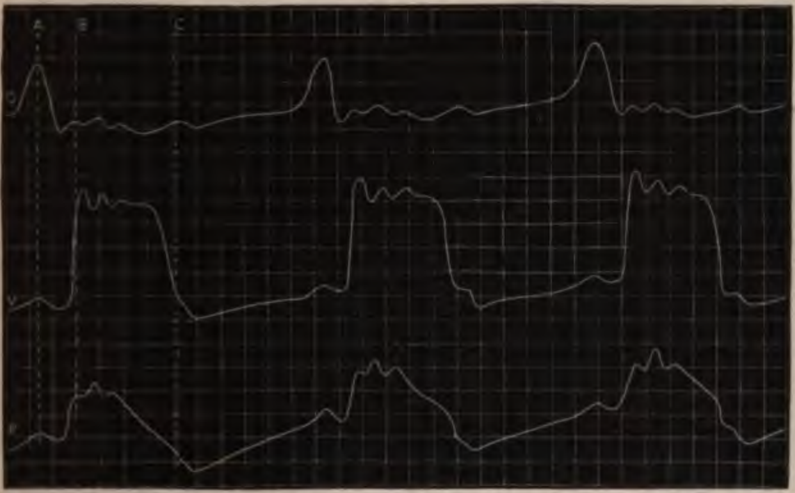

FIG. 60.—Curves of pressure in the right auricle *O*, in the right ventricle *V*, and of the apex beat *P* (horse), after Chauveau and Marey.

At the line C we find almost at the base of the descending limb of both curves a small elevation, which we shall presently discuss further. After the end of systole the ventricle is filled with blood, and the pressure rises slowly up to the succeeding systole. At the same time the cardiogram rises slowly above the abscissa. If the contraction of an empty heart be recorded it has quite another form from that of the cardiogram. From which it is evident that the latter is not a simple contraction curve, but must be regarded as in fact a combined pressure and volume curve of the heart chambers. It is a pressure curve, for the reason that the button placed over the breast wall exerts a pressure against which the heart does work. It is however at the same time a volume curve, in so far as it is influenced by the volume changes of the heart.

While the heart is filling during diastole, the curve rises gradually above the abscissa; but while the ventricles are being emptied, i. e., while the semilunar valves are opened, the pressure against the breast wall is somewhat less and the recording tambour cannot therefore follow the progressive increase of blood pressure.

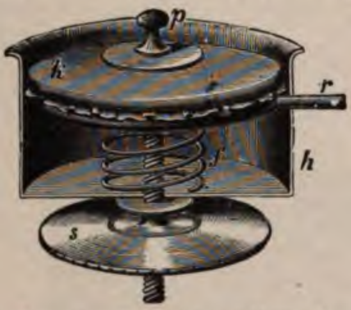

FIG. 61.—Receiving tambour of Marey's cardiograph.

For the graphic registration of the apex beat in man the method of air transmission is generally used, as for example with the apparatus represented in Fig. 61 (*cardiograph* of Marey). A metallic box bears the plunger, *p*, fastened into two small metallic disks, between which the rubber membrane of the tambour is placed. A spiral spring between the inner of these disks and the bottom of the box gives a suitable tension to the membrane. The cardiograph is placed over the thoracic wall in such a manner that the plunger presses on the area of the apex beat. The side tube, *r*, leading out of the box places it in connection with the recording tambour.

It is evident that an apparatus placed over the chest wall in this manner must give a curve which agrees essentially with the one obtained by means of a balloon inserted between the heart and chest wall; for the movements of the chest wall, which is now between the tambour and the heart, are determined by the movements of the heart.

The *human cardiograms* published in the literature show considerable differences in form, depending primarily upon the nature of the recording apparatus employed. From what we know of the possibilities of this apparatus (Hürthle) we may say that the form of the normal cardiogram of man is about that represented in Fig. 62. We have here, as in the animals, an ascending limb, a plateau, which inclines toward the abscissa or runs parallel to it, and a descending limb. Besides there are some small elevations, which in part at least are artifacts.

Often, if not always, the cardiogram begins with a small elevation which is caused by the contraction of the auricle. After this follows the steep rise caused by the contraction of the ventricle. In this case the beginning of the ventricular contraction can be clearly recognized. It may happen however that the auricular contraction is not specially marked, but passes uninterruptedly into the ascent produced by the ventricular contraction, in which case it would be erroneous to reckon the latter from the foot of the ascending limb. This form of the curve results often from too little tension of the cardiograph.

On the cardiogram one sometimes finds at the end of the auricular systole the above-mentioned (page 170) elevation, called by Chauveau the ***intersystole***, which indicates the moment of closure of the atrio-ventricular valves. As a rule, however, the elevation does not occur on the human cardiogram. On the other hand, the moment of opening of the semilunar valves in some cases comes out clearly at the first turning point of the cardiogram, where the ascending limb passes over into the plateau (Fig. 62, *b*). The time interval between the base and the first turning point of the cardiogram, therefore, represents ***the period*** *of rising tension* (period of closure) of the ventricle. This period is not by any means always clearly delimited, and could have but small practical value.

In order to determine the moment of closure of the semilunar valves on the human cardiogram, the heart sounds have been auscultated and marked on the curve by means of an electric signal. The exactness of this method is not great however, and from observations of this kind one can say with certainty only that the second heart sound falls somewhere in the course of the descending limb of the cardiogram. Attempts have been made therefore to determine this moment by other methods.

In man Hürthle and Einthoven have registered the heart sounds automatically in various ways and have found that the second sound comes about 0.02 second after the beginning of the steep descent.

Finally, Edgren has attempted to solve the problem by simultaneous registration of the apex beat and the pulse. Since the pulse wave requires a certain time to propagate itself from the root of the aorta to the place where the pulse is taken, this time must be subtracted. It is then found that the elevation on our cardiogram designated *f* corresponds to a similar mound on the intracardial pressure curve (Fig. 58, *v′*), and corresponds exactly with the well-known dicrotic elevation of the pulse curve. This, as we shall see later, is intimately connected with the closure of the semilunar valves. On this ground it appears justifiable to assert that the mound is produced by the stretching of the semilunar valve.

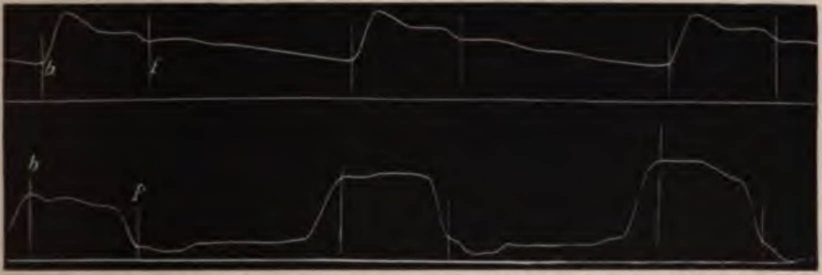

FIG. 62.—Curves of the apex beat (lower line) and of the carotid pulse (upper line) of man, simultaneously recorded, after Edgren. *b*, *b*, and *f*, *f*, are corresponding points.

In so doing we do not wish to assert that the valves are closed then for the first: for that this event transpires much earlier is proved by a comparison of the pressure curves of the ventricle and of the aorta (Fig. 58). It is not improbable that a short time after the noiseless closure of the valves, they are suddenly put on the stretch by the aortic blood acting under great pressure, and that they produce in this way the second sound of the heart. This much is certain, that the second sound cannot begin before the closure of the semilunar valves (shortly after the beginning of the descending limb of the cardiogram) and not later than the mound *f*.

On a typical cardiogram we can make, therefore, a definite determination of the following points: auricular systole, beginning of the ventricular systole; *b*, opening of the semilunar valves, beginning of relaxation; *f*, stretching of semilunar valves.

§ 6. TIME RELATIONS OF THE CARDIAC EVENTS

The duration of the *auricular systole* is very short. In man, as in the horse and dog, it may amount to 0.1 second.

The duration of the *ventricular systole* shows but slight variations, notwithstanding considerable differences in the pulse frequency. Thus in variations between 32 and 124 beats per minute the time occupied by the systole varies only between 0.382 and 0.190 second (man). In animals also where the pulse frequency is made to vary between wide limits by stimulation of the inhibitory and accelerator nerves (cf. § 11) the systolic time varies only a little, whereas the diastolic time presents considerable variations. We may say therefore that the variations of pulse frequency in the same individual as well as in different individuals of the same genus are due in the main to variations in the length of diastole. On the average the length of ventricular diastole in man may be estimated at about 0.4 second.

§ 7. FILLING OF THE HEART IN DIASTOLE

The *most important factor* in the filling of the heart during diastole is the impetus which the heart has given the blood in systole. But since the blood meets with great resistance in its passage through the vessels, the residual driving power is relatively small, and the accessory mechanisms play an important part.

One important mechanism is the suction of the thoracic cavity (cf. Chapter IX). Almost the entire air pressure takes effect on the great veins outside the thorax. A small part of it of course is borne by the skin, etc.; but it may be assumed as certain that the air pressure on the extrathoracic veins is greater than the pressure which is exerted on the organs inside the thorax by the lungs. Consequently in the static position of the thorax the intrathoracic veins and the heart are to a certain extent expanded.

In expiration the negative pressure inside the thorax decreases and both the intrathoracic veins and the auricles become less distended: hence the return flow of the blood into the thorax becomes more difficult. Quite otherwise is it with inspiration. The intrathoracic pressure decreases in direct proportion to the depth of inspiration and to the degree of expansion of the lungs; and since this decrease of pressure is continuous throughout the entire act of inspiration, a continuous expansion of the intrathoracic veins and of the auricles must result, and therefore a direct suction of the blood from the veins to the heart must take place. Under certain circumstances this suction is felt even by the farthest veins.

The return flow of the blood is favored likewise by a static inspiratory position of the chest wall; but in this instance direct suction cannot result, because this would presuppose that the auricles are being continually expanded by extraneous forces, which is not the case unless the chest wall is actually moving.

If the air pressure inside the chest be raised sufficiently the return flow of the blood to the heart is hindered; the circulation stops, and death may result, if the abnormal increase in pressure in the thorax is too long continued.

Furthermore, the heart in its own systole exercises a favorable influence on the return flow of the blood. During systole the volume of the ventricles is diminished by exactly the volume of the blood driven out. This blood is partly taken up by the intrathoracic arteries and the pulmonary vessels, but part of it leaves the thorax. The consequence is that the content of the thorax is smaller. This in its turn produces a suction in the thoracic cavity which acts either to draw air into the lungs through the open glottis (*cardio-pneumatic movement*), or to produce a sinking of the chest wall, or finally to expand the intrathoracic veins whereby blood is drawn into them.

Finally, it has been demonstrated that the heart exercises a suction on the blood in passing into diastole. By means of a minimum valve Goltz and Gaule and others have observed in the open thorax of a dog a negative pressure of 100–320 mm. of water in the left ventricle, 10–25 mm. of water in the right ventricle. Under the same circumstances (open thorax) a negative pressure can be demonstrated in the auricles (De Jager *et al.*).

One succeeds however in demonstrating such a suction only with a vigorously active heart. If the heart movement is weak and if the heart does not empty itself well when it contracts, the suction effect is considerably diminished. What the forces are which bring about this suction is not fully explained.

Excessive filling of the left ventricle is prevented by its thick wall. In the right ventricle the wall is too thin to present sufficient resistance against a very powerful flow of blood, but the danger of overdistention is prevented in part at least by the fact that muscular cords are stretched across the cavity of the right ventricle at different levels.

Moreover the pericardium plays an important rôle, as appears from the following among other observations: a cat's heart held 12 cc. when the pericardium was uninjured, when the pericardium was punctured 11 cc. more could still be driven into the heart (chiefly the right auricle and right ventricle) with the same pressure. Even when beating normally the heart during diastole protrudes through a slit made in the pericardium. Finally it should be remarked that a relative insufficiency in the right atrio-ventricular valve appears after opening of the pericardium. The closure of this valve is insured by the support which the pericardium affords to the heart (Barnard).

§ 8. POWER AND WORK OF THE HEART

A. POWER

We have already seen that the left ventricle in its systole may exert a pressure of 200 mm. Hg. and more on the blood. A weight of this size might then be said to press upon the inner wall of the ventricle. Nevertheless it is able to contract, and its power must be everywhere sufficient to balance such a maximal pressure. In other words, the power of every square centimeter of the internal surface of the left ventricle is equal to the weight of a column of Hg. 1 sq. cm. in section and as high as the maximal pressure expressed in terms of Hg. If we assume that the maximal pressure amounts to 200 mm. Hg., the power of the left ventricle for every square centimeter of its inner surface is 200 mm. × 100 sq. mm. × 13.6[1] = 272 g. It is scarcely worth while to give a value for the total power of the left ventricle, since it is not possible to determine with any accuracy the area of its internal surface during systole. In progressive contraction the residual power of a muscle becomes smaller and smaller. But in the heart this is compensated by the fact that at the same time the internal surface of the ventricle is constantly becoming smaller.

Since the maximal pressure of the right ventricle amounts to about 30 mm. Hg., its power per square centimeter of internal surface would be sufficient to balance 40.8 g.

B. WORK

The work of any chamber of the heart at each systole is expressed by the formula $W = pR + \frac{pv^2}{2g}$, where p is the weight of the output, R is the resistance or mean arterial blood pressure maintained by it, v the velocity per second imparted to the blood, and g the acceleration of gravity.

In order to estimate the work done by the left ventricle, for example, we must determine the pressure and the velocity of the blood in the aorta, as well as the mass of blood driven out at each systole. In the following section we shall go into the subject of blood pressure and velocity in the aorta more fully; here in order to carry out the calculation, we shall say in advance only that the mean pressure may be estimated at about 150 mm. Hg. and the velocity at about 0.5 m. per second.

We cannot say as yet with any definiteness how great is the quantity of blood expelled from the human heart at each systole. It is very probable that the pulse volume is somewhere between 50 and 100 g. per beat. If we adopt these values and substitute them in the above formula, we obtain as the limits of the work necessary to force the blood against the aortic pressure: 50 × 0.150 × 13.6[1] = 102 gram-meters; 100 × 0.150 × 13.6 = 204 g-m.

The work which it requires to impart a velocity of 0.5 meters to the pulse volume is accordingly $\frac{50 \times 0.5^2}{2 \times 9.8} = 0.64$, or $\frac{100 \times 0.5^2}{2 \times 9.8} = 1.28$ g-m. The total work of the left ventricle in its systole would be therefore 102.64 to 205.28 g-m. We see that by far the greater part of the work of the ventricle is used in overcoming the resistance in the vascular system and that only a very small part is necessary to give the blood its mean velocity. This result is perfectly positive in spite of the very arbitrary values used in our calculation, for the pulse volume exercises no influence on the reciprocal relation of the two factors, and even if we estimate the speed in the aorta much higher, and the blood pressure there much lower, the factor pR would still be many times greater than the factor $\frac{pv^2}{2g}$.

We have no direct information as to the quantity of blood expelled from the right ventricle in its systole. But we may assume that its pulse volume is the same as that of the left ventricle; for the left ventricle drives the blood through the greater circulation to the right auricle, and the right drives it through the lesser circulation to the left auricle. Should the two ventricles not expel exactly the same quantity of blood at a systole or in a unit time—we except accidental disturbances—the blood would collect somewhere in the vascular system. Under the assumption that the mean pressure in the pulmonary arteries of man is equal to that of the dog, we obtain for the work of the right ventricle 14.24 to 28.48 g-m.

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[1] The specific gravity of mercury.

In connection with the subject of the blood movements in the arteries we shall discuss more fully how the work of the heart depends upon changes in the vessels and upon their degree of fullness.

§ 9. PROPERTIES OF HEART MUSCLE

A. THE NATURE OF THE CARDIAC CONTRACTION

If the contraction curve of an empty heart be recorded graphically, one observes an unmistakable resemblance to an ordinary muscular twitch produced by a single stimulus. We have in the action current of the heart (cf. page 48) a means of testing this inference. This test can be applied to the human subject also, if symmetrical points of the body's surface be connected with a galvanometer, for the electrical currents generated by the heart's activity diffuse according to the usual laws throughout the entire body (cf. Fig. 63). Fig. 64 represents the action current of the human heart as recorded by the excursions of the capillary electrometer. An upward stroke signifies that the base of the heart is negative to the apex. The ventricular systole begins with the point R; there follows a negative stroke S (the apex negative to the base), and finally, after an interval, a positive stroke T (base negative to apex). From this curve of electrical variations we may infer that the contraction begins at the base and proceeds from there to the apex; for a certain time (a portion of the stretch from S to T) the ventricle is contracted in all its parts, so that the base and the apex exhibit no difference of potential. The contraction ceases sooner at the apex than at the base—which in all probability is due to the return course of the muscular fibers (page 163)—and the base becomes once more negative to the apex. The interval of time between the beginning R and the end T is about 0.32 second, which corresponds fairly well to the duration of a ventricular systole.

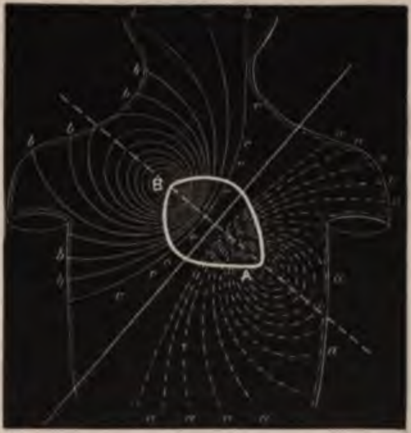

FIG. 63.—Schematic representation of variations of electrical potential associated with the beat of the human heart, and their distribution in the body, after Waller.

From all this it appears that the ventricular systole is comparable with a simple muscular contraction and cannot be regarded as a summated contraction (cf. Chapter XV).

Before the electrical variations corresponding to the ventricular systole a small diaphasic action current is to be observed (Fig. 64, *PQ*), which is probably caused by the auricular contraction. This lasts only about 0.13 second (Einthoven).

B. NUTRITION OF THE HEART

The heart gets its blood supply through its *coronary arteries*, for distribution of which the text-books of anatomy should be consulted. Here it should be recalled only that they do not anastomose with each other, and are therefore *terminal* arteries. Besides, the heart wall obtains blood from the heart cavities through the *veins of Thebesius*, which are in connection with the coronary vessels (arteries and veins) by means of capillaries, and with the veins by means of somewhat larger vessels. The capillary network of the heart is very close, and besides this, the smallest vessels proceed directly from relatively large stems. In those places where several muscle fibers unite, spiral vessels are found which seem adapted to maintain the blood supply when the fibers shift their position and change their form (Heynemann).

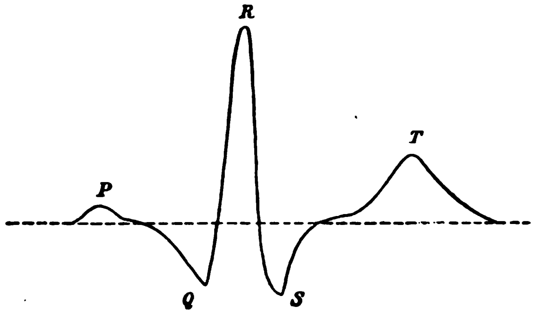

Fig. 64.—Schematic representation of the action current of the human heart, after Einthoven.

The following is to be observed with regard to the behavior of the blood flow through the *coronary vessels* in different phases of the heart's activity. In diastole of the ventricle the vessels of the heart wall are open, and offer no hindrance to the blood stream. When the ventricles contract they must sooner or later exert such a pressure on the capillaries of the heart wall that the blood flow in them is interrupted for a time, and is only resumed at the beginning of relaxation. By this compression of the coronary vessels, blood is driven out into the right auricle. It is found in fact that the quantity of blood flowing in the coronary veins increases during systole. The evacuation of the coronary veins thus brought about has the effect of diminishing the resistance to the blood, so that at the next relaxation they are filled more easily.

This variation in the caliber of its vessels produced by the movements of the heart—to which is to be added possibly a dilatation of the arteries taking place at the beginning of systole—causes a greater quantity of blood to flow through the coronary vessels of a beating heart than of a quiescent one, the quantity being in direct proportion to the force and frequency of the heart beat (Porter, Langendorff). On the other hand the volume of blood flow in a heart suffering from loss of coördination of its muscle fibers may be even greater than in a normally beating heart, which is probably due to the fact that no compression of the coronary vessels now takes place, while the waving movements of the cardiac muscle fibers facilitates the passage of the blood by a [illegible] angendorff). The quantity of blood flowing through the heart is diminished by a greater internal pressure and a consequent distention of the heart, even when it is beating (Hyde).

The flow of blood from the coronary veins is temporarily hindered by the contraction of the right auricle, since at this time the mouth of the common sinus is narrowed—an effect which is aided also by the valve of Thebesius. But the same temporary stoppage tends to favor dilatation of the heart wall, thereby making the auricular systole that much easier. When the auricles relax the coronary veins empty themselves again, and the elasticity of the ventricular wall, which is important for the prompt closure of the atrioventricular valves, can the more readily assert itself (v. Vintschgau, cf. page 166).

Since the coronary arteries do not anastomose with one another, ligation of one of its branches deprives the corresponding part of the heart wall of its blood supply, and a coagulation necrosis then makes its appearance. In such a region the power of contraction is retained however for at least eleven hours; and in animals which survived well the operation of tying off a large arterial branch, the frequency and rhythm of the heart beats and the heart sounds were normal throughout for thirty-six to fifty-four hours afterwards (Baumgarten). Small restricted anæmias were in general well borne.

It is evident that the heart muscle must eventually die, if one of the larger branches of the coronary arteries becomes impassable. What is difficult to explain however is the circumstance that the coördination of the cardiac muscle fibers, upon ligation of a large arterial branch, ceases almost immediately (within one hundred to one hundred and twenty seconds) and the heart falls into *fibrillary contractions*. The same thing happens even if the ligature is loosed before the inception of these disturbances (Cohnheim and v. Schulthess-Rechberg). Since, however, one often meets with cases where such sudden disturbance of the heart's activity does not follow stoppage of its blood supply, it has been assumed by many that this is traceable to some injury to the ventricular wall. Porter on the contrary has shown that fibrillary contractions appear if the blood flow in an artery is stopped in such a way that no possible injury to the ventricular wall can occur, and takes the view therefore that such contractions are caused by scanty nourishment to the heart muscle. That they do not appear in the heart at death from all manner of causes, he explains by saying that the heart is seized with fibrillary contractions only in case it is working against great resistance when the disturbance to its nourishment occurs. When the resistance is not great (and is diminishing gradually) the contractility of the heart muscle decreases steadily, but gradually, and when finally the heart comes to a standstill the residual contractility remaining in it is no longer sufficient to produce well-defined fibrillary contractions. Whether this explanation is correct in all points cannot be definitely decided at this time.

The heart muscle can get its nourishment not only through the coronary arteries but also *through the veins of Thebesius*. From observations on extirpated hearts, it is seen that the food which can be supplied by these vessels is sufficient to maintain rhythmical contractions for a considerable time. The same is true of artificial perfusion through the coronary veins (Pratt).

It has long been known that by artificially supplying blood to the extirpated heart of cold-blooded animals, activity can be maintained for a considerable time (Ludwig). Later Newell Martin and Langendorff accomplished the same thing with the heart of warm-blooded animals. For this purpose blood is led into the aorta by means of a cannula tied in it and directed toward the heart. Because the semilunar valves are closed by the pressure from the cannula, the blood flows through the coronary vessels to the right auricle, whence it is allowed to escape. Numerous observations have been made on such preparations as to the way a heart works under different conditions when separated from the central nervous system and from the blood vessels; and as to the effect which various agents exercise on the performance of the heart.

However it is not necessary to use blood as the nutrient fluid in order to keep the heart beating, for several hours at least; for both in cold-blooded (Ringer) and in warm-blooded animals (Locke) a solution of certain inorganic salts has been found sufficient (0.1 per cent $NaHCO_3$, 0.1 per cent $CaCl_2$, 0.075 per cent KCl, eight per cent NaCl). For the warm-blooded heart the fluid must be saturated with oxygen. By addition of a small quantity of dextrose also this artificial serum is still more effective.

The significance of these substances has been discussed already at page 25. Here it may be added only that the favorable action of the $NaHCO_3$ might be due to the CO_2, for with a sufficient supply of oxygen, carbon dioxide actually increases the energy of the isolated frog's heart (Göthlin).

The great *tenacity of life* exhibited by the exsected heart is truly remarkable. By artificial perfusion with the above-mentioned solution (and dextrose), Kuliabko obtained well-marked contractions of the entire heart of the rabbit five days after the death of the animal. He also succeeded in completely reviving the heart of a four-year-old boy who had died of pneumonia duplex and catarrhus intestinalis, twenty hours after death.

Moreover the tenacity of life in the different portions of the heart is very different. When the heart is dying, the left ventricle stops first, then the right, but the auricles continue to beat for a considerably longer time. Finally the pulsations of the left auricle cease and last of all those of the right. Even then the contractions of the great veins always go on for a time, and only when these have ceased is the heart entirely dead.

When the oxygen supply to the heart is cut off the heart beats become less and less frequent as asphyxiation comes on, and other changes make their appearance which cannot be discussed here. However it should be observed that the heart, especially of cold-blooded animals, has great power of resistance against oxygen hunger (cf. page 28).

C. THE BEHAVIOR OF HEART MUSCLE UNDER DIRECT STIMULATION

If the heart muscle be stimulated with induction currents of different strength, either it does not contract at all, or it contracts to its utmost extent (Bowditch). The response of the heart muscle therefore is always maximal, while the contraction of skeletal muscle is great or small according to the strength of the stimulus. This fact is often referred to as the "all or none" law of cardiac contraction. The crustacean heart (lobster) forms an exception to this rule, since it behaves to stimuli of different strength exactly like skeletal muscle.

Another peculiarity of heart muscle is that in both cold-blooded animals and in Mammalia it is inexcitable during its contraction up to the maximum of shortening—i. e., all stimuli which fall upon it during this ("*refractory*") period are entirely without effect (Marey). Only after the maximum shortening has been reached does the heart muscle become excitable again. A stimulus applied then calls forth an *extra contraction,* which is greater the later in diastole it falls. After this extra contraction a longer ("*compensatory*") *pause* usually occurs, and the first contraction following the pause is considerably augmented. The smaller the extra contraction, the longer is the subsequent pause and *vice versa.* After such an interference in the regular rhythm of the beats, there is therefore a compensation by which both the frequency and the amount of work done by the heart are conserved (cf. Fig. 65).

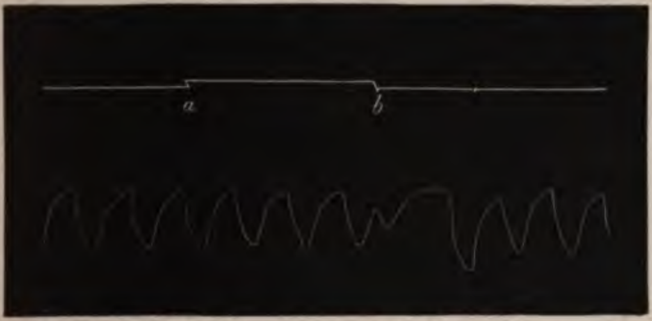

FIG. 65.—Direct stimulation of the isolated heart of the cat while beating, after Langendorff (to be read from left to right; systole represented by the downward stroke). Stimulation at the beginning of systole (*a*) produces no effect. Stimulation at any time during diastole (*b*) gives an extra contraction. Following this are seen the compensatory pause and considerable augmentation in the strength of the next systole.

The compensatory pause appears only in those portions of the heart which beat in consequence of a stimulus communicated to them from other portions; it is not seen therefore in a tracing from the venous sinus of the frog. In explanation of this difference it is supposed that the excitation of the venous sinus is continuous, but that it sends a discontinuous stimulus to the other chambers of the heart. When an extra contraction has been induced in the ventricle, one of these regular discontinuous stimuli from the venous sinus would fall at a time when the ventricle is refractory, hence would produce no effect. The ventricle must therefore wait until the next regular stimulus, and thus we get the compensatory pause. It is quite different with the sinus: as soon as the extra contraction has reached its maximum, the constant stimulus again becomes effective and produces the next systole without an intervening pause.

The inability of the heart muscle to receive stimuli which fall on it during systole, is the reason why with rapidly repeated shocks it *cannot be thrown* *into an actual tetanus,* like skeletal muscles. Since all the stimuli which fall during systole are entirely ineffective, there can be no superposition and summation of effects.

This rule is not strictly without exception, however. By simultaneous stimulation of the vagus and the venous sinus O. Frank was able to demonstrate a condition of tetanus in the frog's heart; Walther observed the same thing on stimulation of a frog's heart poisoned with muscarine. In the latter case the *refractory period* of the heart is shortened as a result of the poison, and the barrier to the production of tetanus is thereby removed.

Many other discoveries have been made on the exsected heart concerning the properties of heart muscle, but they cannot be discussed here. We wish to call attention only to the following peculiarities:

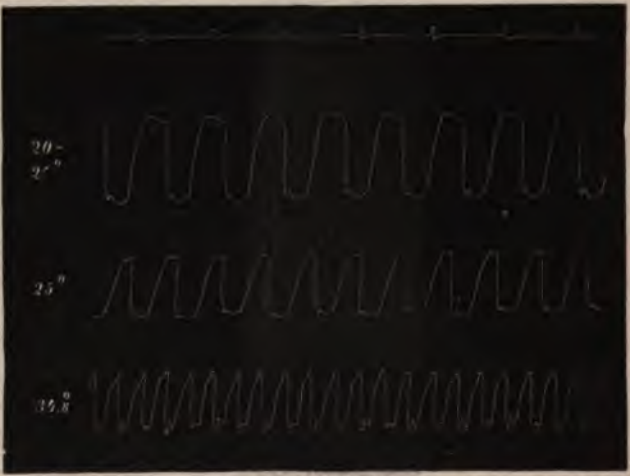

Fig. 66.—Influence of temperature on the isolated heart of the cat, after Langendorff. The heart was supplied with blood kept at the different temperatures indicated.

(1) The frequency of the heart beat *varies directly with the temperature* —i. e., the higher the temperature the greater the frequency, the lower the temperature the less the frequency. Thus at 40° C. it is four times as great as at 15° C. With a fall in the frequency, the extent of contraction increases up to a certain limit, and at the same time the shortening becomes slower and more drawn out (Fig. 66).

(2) The quantity of blood which the left ventricle discharges at each systole depends upon the quantity of flow from the great veins: the greater the inflow the greater the amount discharged, but the latter increases more slowly than the former.

(3) The quantity of blood flowing through the coronary vessels exercises but little influence upon the frequency, although it is of great importance for the force of the heart beat.

(4) If the heart has no work to do it has need of only a very small quantity of blood.

§ 10. THE CAUSE OF THE RHYTHMICAL ACTIVITY OF THE HEART

In warm-blooded animals direct nerve fibers to the auricles as well as to the right and left coronary plexuses, come from the two divisions of the cardiac plexus, which in turn is formed by branches from the vagus and sympathetic. The threads of this network are provided with numerous ganglia, and the fibers radiating to the auricle and ventricle from the network are also interspersed with small ganglia.

In the heart itself *ganglion cells* have been found in the following places: in the auricles around the opening of the great veins, along the periphery of the septum, and, though in smaller number, in the outer wall; in the atrioventricular groove, especially in the region of the aorta and pulmonary artery at the level of the semilunar valves; and in the uppermost part of the ventricle.

Fine nervous nets supply an abundance of nerve fibers to all parts of the heart.

As appears from what has been said concerning exsected hearts, this organ possesses the property of acting quite *independently of the central nervous system*. In order to determine the cause of this peculiarity we have to investigate first the behavior of the separate divisions when they are isolated from the whole heart. In this we shall consider chiefly the phenomena appearing in the Mammalian heart, because a detailed discussion of those observed in the hearts of cold-blooded animals would call for entirely too much space.

By introducing into the auricle a small instrument provided with curved plates on two sides, it is possible to sever all the nervous and muscular connections between the auricles and ventricles without producing hemorrhage. After this operation the ventricles continue to pulsate without interruption.

In this experiment the line of separation can be brought close to the auricular boundary. Since now all the nerves which run to the heart along the great arteries are afferent in function (Wooldridge), and since the results are the same in case the great arteries are pinched off directly above the upper edge of the semilunar valves, it follows that the isolated portion of the heart, i. e., the ventricles and a very small part of the auricles, have within themselves all the conditions necessary for rhythmical activity.

One can go still further. Porter has succeeded by means of artificial circulation through the coronary arteries in maintaining regular rhythmical contractions in isolated pieces of the ventricular wall, connected with the rest of the heart only by the arterial branch. We can extend the proposition stated above therefore, and say that *every portion of the ventricular wall possesses all the conditions necessary for rhythmical activity.*

In these experiments one meets with cases where the rhythm of the separated portion is materially less than that of the whole heart or that of the divisions remaining after isolation of the ventricles. But under normal circumstances the rate of the ventricular systole is determined by the rhythm of those parts of the heart which inaugurate the systole (the venous ostia of the auricles; cf. page 162).

It is most probable that we have to do here with a *chemical stimulus* of some kind, which is to be sought among the products of decomposition formed in the activity of these parts. If this is so, it follows that the inorganic constituents which, as mentioned above, must be present in an artificial fluid in order to maintain the heart's activity, and which occur in the blood, are not to be considered as the real excitant of the heart beat, but merely as a condition.

Since the structure of cardiac muscle agrees essentially with that of skeletal muscle, and the latter is set in action normally only under the influence of a stimulus communicated to it from the central nervous system, it was for a long time supposed that the rhythmical contractions of the heart were not caused by any specific property of the muscle fibers, but were discharged by *intracardial ganglion cells.* This view found weighty support in the fact that these cells were demonstrated in just those parts of the heart where the systole begins. In more recent times various authors, notably Gaskell and Engelmann, have advocated the view that the spontaneous contractions of the heart are of muscular origin, and are due to a *special property of cardiac muscle.*

The following facts among others have been adduced as arguments for this conception. The venous sinus in the frog contains a large collection of ganglion cells, known as Remak's ganglion, which on the ganglion hypothesis has often been referred to as the originator of the heart beat. Now it has been found that normal pulsations can be started from every other place in the sinus region; the sinus ganglion is not, therefore, absolutely necessary. In the frog in the normal course of events, the contraction waves probably proceed not from the sinus but from the great veins. These pulsate spontaneously if they are isolated entirely from the rest of the heart, even if the isolated portion contains no ganglion cells. The same is true of the bulbus arteriosus of the frog's heart, in which no ganglion cells are present. Moreover in the heart of the higher invertebrates, and in the spontaneously contractile veins of the bat's wing, notwithstanding diligent search, no ganglion cells have been found. Again the embryonic heart of mammals beats in a perfectly characteristic manner at a time when no nerve or muscle cells have yet been differentiated.

All these and still other circumstances go to show that a rhythmical, automatic activity of contractile tissue can be brought about without the participation of ganglion cells; and it is, therefore, possible that the automatism of the fully developed vertebrate heart is of muscular origin. The great tenacity of life of the heart speaks strongly for this view also; for from all that we know of ganglion cells elsewhere, they perish in much shorter time than is required for the exsected heart to lose its power of rhythmical contraction.

The fact that this power is developed to different degrees in different parts of the heart, and that individual parts, like the clamped-off apex of the frog's ventricle, will never pulsate spontaneously under the influence of the normal stimulus, is explained according to the muscular theory by supposing that automatism, originally common to all the cardiac muscle cells, has disappeared in the course of development from some places, notably the apex, but remained in others, notably the region of the venous sinus.

The number of authors who have taken the side of this hypothesis has constantly increased—a fact not difficult to understand in view of the great logical precision with which it has been developed. Nevertheless it appears that there are still certain difficulties to be overcome. For example, the questions: how it transpires that the venæ cavæ and the pulmonary veins, although separated by a considerable distance, are roused to action simultaneously; and how the normal coördination of the heart muscle, as well as the disturbances of the same by electrical stimulation, by anæmia and by mechanical abuse (cf. page 183), are brought about have not yet been satisfactorily answered.

Any explanation of the origin of the contraction must take account also of the question as to *how the excitation is propagated* through the heart, whether through the musculature itself or through a set of nerves; because, if the muscular theory of the heart beat is correct, it follows almost of necessity that the propagation of the stimulus is muscular, and *vice versa.*

If the ventricle be artificially fed by the coronary arteries, and be divided up into different parts connected together by the arterial branches, and joined by thin muscular bridges, all the portions beat synchronously, no matter in what direction the cuts are made. After section of the muscular bridge, the synchronism stops and each part beats after its own rhythm, but does not show any signs of fluttering (Porter).

Neither these phenomena nor the corresponding observations made on the frog's heart are, however, to be regarded as conclusive proof of the muscular theory of propagation, inasmuch as the cardiac muscle fibers themselves are surrounded by nerves which could only be excluded by complete division of the last muscular bridges, and might therefore cause the synchronism.

The passage of the excitation from the auricles to the ventricles once constituted a serious difficulty in the way of a muscular theory. It was supposed that the musculature of these two divisions were completely separated. It has been shown, however, that direct muscular connections are indeed present between the two (Kent, His, Jr.), and the excitation might therefore pass from the auricle to the ventricle without any participation of nerves.

As mentioned above, a certain time intervenes between the auricular and the ventricular systoles. From the standpoint of the ganglion hypothesis this delay would not be difficult to explain, since we know from many other observations that ganglia in general do delay the propagation of impulses. But the muscular theory also has been able to offer an explanation by supposing that the transmission of the motor stimulus takes place very quickly within each separate division of the heart, while over the cells which form the connections between the separate parts, the transmission is very slow, just as it would be over smooth or embryonic muscles.

What appears to disprove conclusively the hypothesis of nervous propagation, and is therefore a very weighty support for the muscular hypothesis, is the following. If the auricle of a frog's heart be injured by a light pinch, the rhythmic excitation travels just as before over the entire heart. But if the vagus be now stimulated, as long as the inhibitory action lasts, the ordinary excitation passes only up to the injured spot and stops there. If the propagation were through a nervous mechanism, we should have to suppose that the conductivity is temporarily abolished exactly at the injured place (F. B. Hofmann), which however could only be explained by an action of inhibitory fibers on motor fibers. Such effects are entirely unknown elsewhere and are therefore extremely improbable here. The phenomenon presents no special difficulty, on the other hand, if we suppose that the transmission is purely muscular, and has been rendered impossible by the action of the inhibitory nerves on the injured muscle.

The synchronism of the two ventricles is not effected by simultaneous impulses from the auricles, but by their muscular or nervous connection with each other. For if the two be separated from one another, but be left in connection with their respective auricles, the synchronism is broken and each beats in its own rhythm (Porter).

§ 11. THE EFFERENT CARDIAC NERVES

The activity of the heart is controlled by impulses from the central nervous system brought to it over the *vagus* and *sympathetic* fibers. Afferent nerves also pass to the brain from the heart, and these influence both the heart itself and the blood vessels of the general system reflexly. The rich supply of nerve fibers to the ultimate muscle fibers of the heart are the terminal branches of these same nerves.

The importance of these regulatory influences can scarcely be overestimated. This is well shown by the following observations of Friedenthal on a dog, whose extracardiac nerves were all cut, the afferent fibers from the lungs, and the fibers to the stomach and the œsophagus being preserved on one side. The animal, which had survived the last operation for more than eight months and had then succumbed to acute strophanthus poisoning, showed in the meantime on superficial examination scarcely any abnormality. The number of heart beats, for example, was not noticeably changed. When, however, the animal was required to run, the abnormality became very apparent. Although he had recovered his original weight within two months of the operation, he was unable afterwards to run half a mile. The ability to do even a moderate amount of work had therefore been lost, because the mechanism for increasing the heart action was wanting.

A. THE INHIBITORY NERVES

If the vagus be cut in the neck and its peripheral end be stimulated with tetanizing induction shocks, *slowing of the heart beat or complete diastolic standstill*, according to the strength of stimulation, results. The vagus therefore inhibits the heart movements. We owe this important discovery to the brothers, E. H. and E. F. Weber (1845).

If both vagi of an animal be cut, the heart immediately beats faster. Under normal circumstances therefore *a constant restraint* is being exercised by the central nervous system upon the heart, in consequence of which it beats more slowly than it otherwise would.

The vagus influences not only the *frequency* of the heart beats, but also the *force*. In fact it may happen under certain circumstances that when the vagus is stimulated the pulse frequency remains entirely unchanged, while the size of the contraction becomes constantly smaller (Heidenhain, Gaskell). According to Muskens, this takes place in the frog and turtle only in the excised heart or after loss of blood. The heart relaxes in diastole more during vagus stimulation than otherwise, but this might be caused by the longer pause, affording more time for relaxation (O. Frank, F. B. Hofmann).

The following observations have been made with regard to the way in which the vagus acts upon the different divisions of the mammalian heart. The inhibiting influence extends not only to the heart itself, but also to the central veins, so that their contractions may completely cease on vagus stimulation (Knoll). With reference to the auricles it is unanimously asserted that it is the force of contraction which is primarily diminished, and that it may even happen, in spite of a considerable decrease in the extent of the contraction, that the rhythm remains entirely unaltered. On the other hand, it invariably happens that a fall in frequency is accompanied by a reduction in the size of the contraction.

Results differ somewhat as to the behavior of the ventricles. It seems, however, to be pretty certain that with weak stimulation where the heart beats are not retarded very much, the contractions of the ventricles are somewhat stronger than otherwise; and that with stronger stimulation and considerable retardation the contractions become weaker. The augmentation in the first instance need not be a direct effect of the vagus, for it may be due to the fact that with a slower cadence a greater volume of blood is at the disposal of the heart at each systole; besides, it must not be forgotten that with the longer diastole the blood pressure in the arteries must fall, so that the heart has less resistance to overcome.

The cause of the reduction in frequency, or the complete standstill of the ventricle effected by the vagus is to be sought in a direct effect on the ventricles themselves. One would think that when the auricles are stopped they would no longer discharge impulses to the ventricles. While this is possible it does not seem very probable, at least for the mammalian heart, for under certain circumstances the ventricles may beat at the rhythm of the great veins while the auricles are perfectly quiescent (Knoll). Besides, the power of the ventricles to beat rhythmically when isolated from the auricles is so great that mere stoppage of the auricles may not necessarily affect the ventricles. Vagus retardation may, however, be brought about in such a way that the impulse cannot be propagated from auricles to ventricles. Thus there are cases where the auricles beat at a more rapid rhythm than the ventricles, although the excitability of the latter is not diminished in the least. Finally, it has been shown that when the heart is brought to a complete standstill by strong vagus excitation, the cardiac muscle is less excitable to direct stimulation and cannot be roused to contractions so extensive as is normally the case. All of which bears out the statement that the vagus acts directly on the ventricular muscle.

Engelmann describes these effects of vagus excitation as negatively *chronotropic* (retarding), negatively *inotropic* (weakening), negatively *dromotropic* (diminishing the conductivity), and negatively *bathmotropic* (reducing the irritability); and is inclined to the assumption that they are brought about by four special sets of nerve fibers. This conception, based on the frog's heart, receives some support from Pawlow's observations on the stimulation of separate fibers in the cardiac plexus of the dog, according to which either the force or the frequency of the heart beat could be influenced either in a positive or negative direction, according to the fibers stimulated. Other authors take the view that the inhibitory nerves consist of only one set of fibers, and that the different effects depend upon their condition at the time of stimulation. A definite decision of the matter is not possible at this time.

The view has often been expressed that the vagus influence on the heart is of a *nutritive* or *trophic nature*. The following facts might be construed in favor of such a view: the strength and working power of the heart, as well as the ability of the heart muscle to propagate a stimulus, increases after vagus stimulation; the heart's activity, if it is weak, is materially raised by vagus stimulation; and in the asphyxiated animal the heart beats longer if the vagi are left intact, than if they be cut, etc. But these phenomena might be explained also by the longer resting period after each systole.

Conclusive proof of the correctness of this view would be afforded, if degenerative changes could be demonstrated on a heart whose vagi had been cut. Such have in fact often been mentioned, and it has even been asserted that they are confined to different parts of the ventricles, according as the right or left vagus is cut. But we have the researches of Pawlow and Friedenthal to the contrary. They find that the heart of dogs which had survived bilateral vagotomy for several months presented no anatomical changes whatsoever. The long time during which the animals remained alive in these researches, as well as in those of Nikolaïdes and Ocaña, itself goes to show at least that the vagus cannot be exclusively a trophic nerve for the heart.

That the inhibitory process is, nevertheless, accompanied by demonstrable molecular changes, and that the stoppage is not therefore a kind of paralysis, appears from the electrical variations in the heart muscle which accompany vagus stimulation. In the turtle's heart it is possible to separate the auricles from the venous sinus without injuring the nervous fibers of the former. The auricles stop for a time. If now the apex be killed by immersion in hot water, and both base and apex be then led off to a galvanometer, the usual demarcation current is observed with the injured spot, i. e., the apex, negative toward the base. If the vagus is stimulated the auricles remain at rest; but the galvanometer shows a positive variation (Gaskell). This variation of the animal current is evidently opposite in sign to that which takes place in the work of the heart muscle (cf. page 179). Fano obtained quite similar results when he stimulated the vagus of an active turtle heart so feebly that it was not stopped but only retarded. The positive phase of the variation was increased, but the negative was diminished or abolished altogether.

Since now the negative variation is quite certainly the expression of a dissimilatory process, one would be forced by the appearance of a positive variation on stimulation of the vagus to the conclusion that this nerve calls out processes of a synthetic nature. If, however, this is true, it follows from the above observations on vagotomy that these synthetic processes are not of critical importance for the maintenance of the normal structure of the heart.

In discussing the intracardial innervation of the heart (page 186), the significance of the ganglia was left an open question. It will be appropriate to revert to the subject here, because some observations on the vagus should be able to give the desired answer. Langley has shown that nicotine puts an end to the transmission of an impulse through the sympathetic ganglion cells with which the nerve fibers (preganglionic) coming from the central nervous system are connected, whereas the fibers (postganglionic) arising from these cells retain their excitability (cf. Chapter XXV). This method has been employed also for the study of the ganglionic connections of the vagus fibers. In a frog poisoned with nicotine, stimulation of the vagus trunk produces no inhibition of the heart; but stimulation of the nerves running in the auricular septum under certain circumstances gives very marked weakening of the heart beat. The ganglion cells of the venous sinus must therefore be regarded as a relay station for the cardiac inhibitory fibers (F. B. Hofmann).

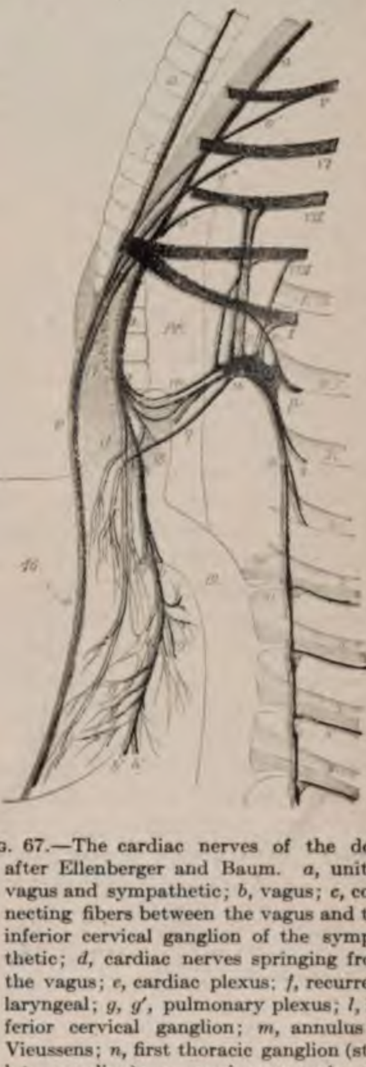

Fig. 67.—The cardiac nerves of the dog, after Ellenberger and Baum. *a*, united vagus and sympathetic; *b*, vagus; *c*, connecting fibers between the vagus and the inferior cervical ganglion of the sympathetic; *d*, cardiac nerves springing from the vagus; *e*, cardiac plexus; *f*, recurrent laryngeal; *g*, *g′*, pulmonary plexus; *l*, inferior cervical ganglion; *m*, annulus of Vieussens; *n*, first thoracic ganglion (stellate ganglion); *o*, rami communicantes from this ganglion to the lost cervical nerves; *p*, rami communicantes to the first and second thoracic nerves; *q*, cardiac branch from the stellate ganglion; *r*, trunk of the sympathetic in the thorax; *s*, rami communicantes to the spinal nerves; *s′*, intercostal nerves; *v*, phrenic nerve; 16, heart; 17, innominate artery; 18, left subclavian vein; 19, aorta.

B. THE ACCELERATOR NERVES OF THE HEART

These arise from the sympathetic (Fig. 67). They pass out of the spinal cord in the upper four or five (most of them in the second and third) thoracic spinal roots, and run in the sympathetic chain to the first thoracic ganglion (*n*). The latter sends out two connecting branches to the inferior cervical ganglion (*l*), or to the vagus (*a*), which run on either side of the subclavian artery forming the annulus of Vieussens. Either from the inferior cervical ganglion itself, or from the annulus, or from the trunk of the vagus just below the inferior cervical, *the accelerator nerves* (*g*) are given off to join the cardiac plexus. Besides, accelerator fibers are found in the cervical portion of the vagus, since with the inhibitory fibers thrown out of function by atropine poisoning vagus stimulation produces an acceleration of the heart beat. The accelerator fibers running in the sympathetic are described by physiologists as the accelerator nerves.

Stimulation of the accelerator increases the pulse frequency more or less (v. Bezold, the brothers Cyon) according as the frequency was previously low or high. The absolute maximum of frequency attainable by stimulation of the accelerator mechanism is *entirely independent of the previous rate*

(Baxt). The increase is accomplished mainly by shortening the diastole. When stimulation has ceased an *after-effect* remains which in favorable cases lasts for as much as two minutes.

Just as with the inhibitory nerves, the accelerators appear to exercise a *tonic influence* on the heart. Evidence for this we have in the fact that bilateral extirpation of the lowermost cervical and uppermost thoracic ganglia, after section of both vagi, diminishes the pulse frequency. The normal rate of the heart beat therefore is determined by the accelerator nerves as well as by the inhibitory, and it appears from Friedenthal's results, given on page 188, that the former are just as necessary for the heart's activity as the inhibitory nerves.

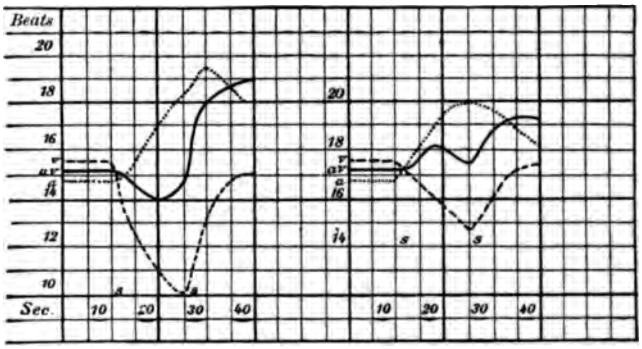

Fig. 68.—Graphic representation of the pulse rate: *v*, on stimulating the vagus; *a*, on stimulating the accelerator nerves; *a v*, on stimulating both simultaneously, after Hunt. Stimulation lasted fifteen seconds in each case, *s—s*.

The size of the auricular and the ventricular contraction in most cases increases upon stimulation of the accelerator. But it may happen also that the extent of the contraction increases, while the heart frequency is not influenced at all, and, vice versa, acceleration may take place without any increase in extent. In any case these nerves improve the execution of the heart and heighten the dissimilatory processes going on within it; hence the proposed designation of them by Hofmann as the *promoting nerves* in contradistinction to the inhibitory nerves, very aptly characterizes their properties.

By way of analogy with his conception of the inhibitory nerves of the heart, Engelmann supposes that the accelerator nerves also have several kinds of fibers: positively chronotropic (increasing the rate); positively inotropic (increasing the force); positively dromotropic (increasing the conductivity); and positively bathmotropic (increasing the excitability). The same comment would apply to this conception as to that concerning the inhibitory fibers (page 189).

It has been found, mainly by the use of the nicotine method, that the "promoting fibers" also unite with intracardial ganglion cells.

With regard to the *antagonistic relations* of the vagus and accelerator, experiments show that the one nerve or the other predominates according to the relative strength of its stimulation, and that with a stimulus of suitable strength for each, the two effects may be made to balance each other so that both the rate of the heart beat and the duration of its different phases may remain almost entirely unchanged (Bayliss and Starling, O. Frank, Hunt, *et al.*).

And yet we are not to suppose that the resultant effect is the algebraic sum of the two when acting separately. For upon stimulation of the two together, if the vagus effect predominates during stimulation, a characteristic after-effect of the accelerator comes on when stimulation has ceased (Fig. 68). The two nerves are not therefore to be regarded as true antagonists; for if they were, stimulation of the two ought to give the same result as stimulation of neither; that is, the peculiar after-effect of the accelerator ought not to appear (Baxt). In view of these facts, it seems probable that the inhibitory and "promoting fibers" have different modes of connection with the cardiac muscle fibers.

§ 12. THE HEART REFLEXES

The efferent cardiac nerves are roused to action reflexly both by the afferent nerves of the heart itself, and by other nerves, and the heart is variously influenced.

On the anterior as well as on the posterior wall of the ventricle run numerous nerves, which, on stimulation of their central cut ends, reflexly raise or lower the blood pressure, and accelerate or retard the rate of the heart beat (Wooldridge). The heart itself therefore through its own afferent nerves can set in action mechanisms by which the circulatory apparatus can be changed in one sense or the other, according to the momentary requirements.

The *depressor nerve* discovered by Ludwig and Cyon, which runs as a separate nerve in the rabbit, is the most important of the nerve trunks conveying fibers *from* the cardiac plexus. It rises as a rule by two roots, one from the cervical portion of the vagus, the other from the superior laryngeal, and runs parallel with the vagus to the cardiac plexus (Fig. 69). According to Koster and Tschermak, the depressor does not come from the heart but from the aorta. Because of its great importance for the action of the heart, we shall discuss it in this connection.

Stimulation of its peripheral end has no effect whatever. Stimulation of the central end produces a fall in blood pressure and retardation of the heart beat (Fig. 70). If the vagi are cut the latter effect is wanting, but the fall in pressure occurs just as before. The retardation is therefore due to reflex

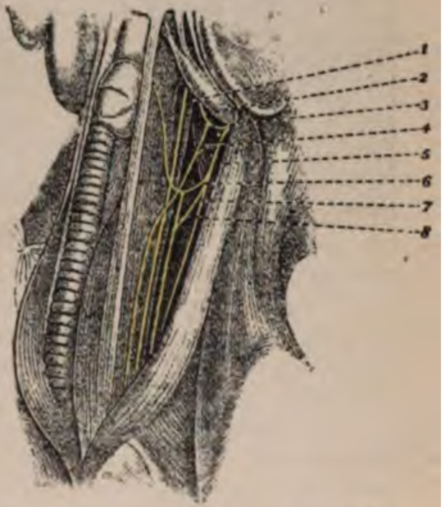

FIG. 69.—The depressor nerve of the rabbit, after Ludwig and Cyon. 1, sympathetic; 2, hypoglossal; 3, descending branch of the hypoglossal; 4, branch from the cervical plexus; 5, vagus; 6, superior laryngeal; 7, first and 8, second root of the depressor.

excitation of the vagus, the fall in pressure to a reflex dilatation of the blood vessels.

The natural assumption with regard to the normal action of the depressor, is that it is stimulated by dilatation of the aorta, when for example the pressure there becomes very high so that it is difficult for the heart to empty itself. The blood vessels are dilated as the result of the depressor impulses, and the heart, working now against less resistance, empties itself more easily. Since the heart beats more slowly also as the result of the vagus reflex, it has a better opportunity to recover after the previous overexertion. These conclusions have been confirmed by recent observations; e. g., when high pressure is produced artificially in the arch of the aorta, an action current appears in the trunk of the depressor (Tschermak), and if both depressors are cut when the pressure is high, the pressure rises still further (Pawlow).

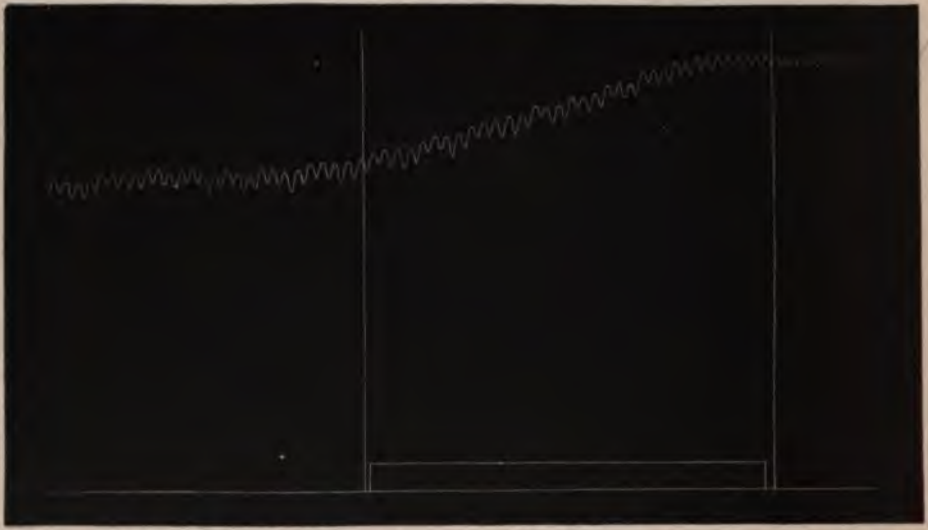

FIG. 70.—Behavior of the blood pressure on stimulation of the depressor nerve. To be read from right to left. The two vertical lines indicate the time of stimulation. ⌐‾‾‾‾‾‾‾¬ = ten seconds.

According to Cyon, the depressor has a *third root*, central stimulation of which produces an acceleration of the heart; this root is connected with the superior cervical ganglion.

The heart does not appear to have nerves which mediate tactile sensations; on the other hand reflexes may be started from its afferent nerves which take effect in the skeletal muscles.

The heart may be influenced reflexly by a great many other nerves. If one vagus be cut, and the other be left intact, central stimulation of the cut nerve produces a slowing of the pulse, which disappears when the other is cut. Among the different afferent fibers of the vagus, those coming from the lungs are most effective, those from the heart much less so, and those springing from points below the lung fibers are still less effective (Brodie and Russell). The inhibitory nerves of the heart are excited also by stimulation of the central end of the *superior laryngeal*, of the *splanchnic* and of the *trigeminal*.

Acceleration is obtained by *inflation of the lungs*; and in man it has been found that any increase of intrabronchial air pressure, as in speaking, singing, rapid and forced respiration, etc., accelerates the heart beat.

The effect on the heart of central stimulation of sensory nerves in the strict sense, as well as nerves of the special senses, is twofold: either an acceleration or a slowing. Only the trigeminal gives an invariable retardation; stimulation of the nasal mucous membrane stops the heart immediately. It is possible that the result of stimulation depends upon its strength, inhibition following strong, acceleration following the weak current. We may also suppose that such nerves consist of two kinds of fibers, one of which brings about inhibition of the heart beat, the other acceleration; but this is improbable. The afferent nerves from the muscles appear to exercise but a slight influence on the heart.

Although the heart reflexes have not been studied at all sufficiently, we may affirm with a moderate degree of certainty that acceleration as well as inhibition of the heart beat can be brought about reflexly by a great many afferent nerves.

Inhibition is certainly to be regarded as a reflex carried over to the vagus, as appears unequivocally from the fact that when both vagi are cut the heart beats faster. It is generally supposed also that acceleration is mediated by reflex excitation of the accelerator nerves. However, Hunt has made some researches from which he concludes that reflex acceleration is caused by a reduction in the tonus of the inhibitory center, and he has endeavored with great skill to prove that in most cases of augmented heart action the cause inheres in this rather than in excitation of the accelerator, although he admits that augmentation is stronger with uninjured accelerators, than when these are destroyed, because with diminshed tonus of the vagus they can act on the heart more powerfully.

§ 13. THE CARDIAC NERVE CENTERS

We designate as the *center of a nerve*, that place in the central nervous system from which its activity is influenced either automatically or reflexly.

Nothing definite is known about the location of the *augmentor center* for the heart. But since a stimulus applied to the upper part of the medulla produces acceleration of the heart beat, it is natural to locate this, with the other vegetative centers of the body, in the medulla.

It is perfectly certain that the *inhibitory center* is in the medulla. A needle puncture halfway up the medulla and pretty well to one side, causes slowing and stoppage of the heart.

The cardiac nerves are influenced also by portions of the brain anterior to the medulla, including even the cerebral cortex. This is confirmed by our daily experience that the psychic states—joy, fear, hope, etc.—increase or diminish the frequency of the heart beat. Most persons, however, find it impossible to influence these centers by direct effort of the will.

The frequency of the heart beat can be changed in one direction or another by the so-called *motor areas* of the cerebral cortex and by different lower parts of the brain. But it is not correct to regard these portions as the seat of the active centers of the cardiac nerves. It seems preferable to regard the cerebrum, etc., as peripheral organs by which the cardiac centers are excited reflexly, just as they are roused to activity by afferent fibers coming from other parts of the body (Franck). According to this conception the actual center of the inhibitory nerves would lie *only in the medulla.* It can be acted upon by a great many afferent nerves—from the skin, from the heart itself, from the abdominal viscera, the lungs, the sense organs, and from the different parts of the brain.

The blood pressure also exercises an influence on the rate of the heart beat. It is true that in an exsected heart, one observes no influence upon the pulse-frequency by variations of the arterial pressure within the vital limits, and the variations of the pulse produced by great variations of the venous pressure are not especially large. But under normal conditions of the circulation, very evident changes in frequency often occur as the result of variations in pressure, and this even if every possible connection of the heart with the central nervous system is broken. Thus it is found that if an increase in blood pressure due to a local vasoconstriction occurs, there often goes with it an acceleration of the heart beat, the chief cause of which is probably to be sought in the suddenly increased blood supply to the heart. By this means those portions of the heart where the contraction starts are roused to more frequent action.

In a heart completely isolated from the central nervous system an increase of pressure may produce also a retardation. The inhibitory mechanism therefore as well as the motor mechanism can be excited by a rise of blood pressure. The result will depend upon the relative irritability of the two mechanisms.

When all the cardiac nerves are intact, the heart frequency decreases with a rise in blood pressure and increases with a fall, whatever the order in which the variations succeed each other. Since slowing of the heart is not the usual result of increased arterial pressure when the vagi are cut, it is clear that the above-mentioned phenomenon is an effect of the *vagus center.*

This excitation of the vagus center is called out in part by the depressor; but is probably also connected with a change in the circulation of the brain, excitation of the center following an increase of intracranial pressure.

Nothing certain is known as to how the accelerator center acts with a rise of pressure. The increase of pulse frequency observed in an anæmic condition of the brain might possibly be referred to an excitation of this center, but it can be explained also by a fall in the tonic influence of the vagus center.

From the facts just discussed, it cannot be looked upon as fully established that effects on the efferent cardiac nerves, which can be obtained by stimulation of afferent nerves, are caused exclusively by a reflex from the cardiac centers, for it is not impossible that a change in the blood supply to the brain, brought about by a reflex effect on the vascular system, has participated to some extent.

§ 14. THE RATE OF HEART BEAT

Now that we have studied the influence of nerves upon the rate of the heart beat, it remains for us to inquire what are the *normal variations in man.*

If all disturbing influences be removed as far as possible—i. e., if the individual be resting quietly in bed and abstain from food—only very slight variations in the pulse frequency appear in the course of the day. But the pulse rate is quickly affected by all sorts of influences.

Heavy bed clothing sufficient to produce a growing sensation of warmth quickens the pulse frequency considerably. Exposure of the naked body to air at a low temperature reduces the rate; but if the temperature of the air is high the rate rises. Hot and cold drinks have the same effect as external temperature: drinking hot water accelerates, drinking cold water retards the pulse. A burning sensation or sensation of pressure, etc., in the stomach or intestine quickens the pulse.

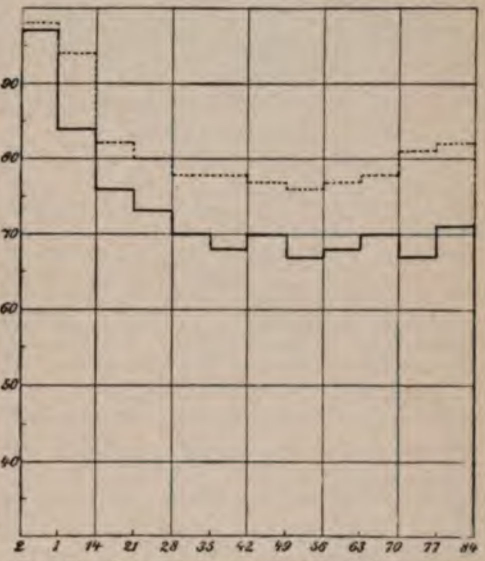

Fig. 71.—The pulse rate in man at different ages, after Guy. ———, males; ---------, females.

Under such circumstances it is evident that a *meal* may exercise an important influence on the pulse frequency, and this is confirmed by experience. The pulse rate as a rule is higher at meal times, owing mainly to the addition of heat to the body.

Bodily movements exercise the most profound influence on the pulse rate, and we can almost say that the rate increases in direct proportion to the *effort* required and the extent and *vigor* of the movement. Detailed experiments are at hand showing that the increase is due in small part to a direct effect of products formed in the muscular activity on the heart itself, but in by far the greater part to the fact that along with the voluntary impulses from the higher brain centers to the muscles there go also involuntary impulses to the cardiac centers, whereby the tonus of the inhibitory center is diminished or the accelerator center is excited (Johansson; cf. page 195).

Figure 71 shows how the pulse rate varies with *age*. In the first year it is highest; it then falls to a minimum of about seventy per minute near the twentieth year (for males), where it remains until the approach of old age, when it again rises somewhat.

The higher pulse rate in children is due in part to the smaller *size of the body*, just as we find in grown animals of different species that the large ones have a slow pulse, the small ones a rapid pulse (e. g., horse and ox 36 to 50, rabbit 200 per minute). This difference is without doubt connected with the relatively more active metabolism of small and young individuals (cf. page 117 *et seq.*).

Figure 71 also furnishes information with regard to the influence of *sex*. The pulse frequency for all ages above two years is higher in the female than in the male. The smaller size of the female body is the most important factor in this difference. One finds on comparison of the pulse rate in men and women of the same height that it is somewhat higher in the latter, but the difference is much less than when male and female individuals of the same age, without regard to size, are compared.

Again we meet with considerable variation of pulse rate in *different individuals*, a very low (26–20 per minute) and a very high rate (120 per minute) having been observed in men of perfectly sound health.

THIRD SECTION

THE BLOOD FLOW

§ 1. THE FLOW OF A LIQUID IN RIGID TUBES

If a reservoir be so arranged as to deliver a liquid through a tube of uniform diameter as represented in Fig. 72, the mean velocity of the flow will be the same in every cross section of the tube. This follows from the fact that fluids are not compressible. Moreover, the internal friction of the fluid creates a resistance which causes it to flow more slowly than it would if it were pouring directly from an opening in the reservoir; and in consequence of this friction the liquid in the tube is subjected to a tension, which, however, is smaller than it would be if the flow from the end of the tube were hindered in some way. This tension manifests itself as a lateral pressure which can be measured by means of vertical tubes leading off at intervals along the delivery tube. If the highest points of the columns of liquid be connected with each other, a straight line is obtained—i. e., the lateral pressure decreases uniformly in the direction of the current, to the end, where it is nil. The lateral pressure at any given point along the delivery tube is equal to that part of the whole pressure which is necessary to overcome the resistance of the current from that point onward.

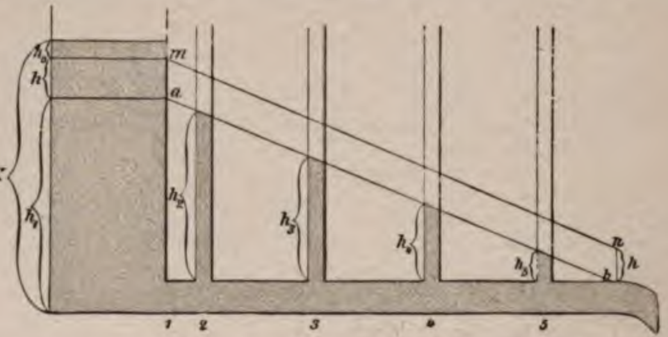

FIG. 72.—The flow of a liquid through a rigid tube of uniform diameter.

If the system through which the liquid flows consist of a number of tubes of different diameter fastened together, as in Fig. 73, the same fundamental laws hold good. Because the liquid is not compressible the same quantity must flow through every cross section of the tube, whatever its size, in unit time. Consequently the velocity in the different sections of the tube stands in inverse relation to their cross section. The lateral pressure within the different sections falls at different rates—most rapidly in the narrowest, most slowly in the widest. In sections of the same diameter, whether they are separated by narrow or wide portions, the fall in pressure is the same, for the velocity and hence the internal friction also, are the same in these.

When a main-delivery tube is divided up into a number of small branches, whose total cross section area is greater than that of the stem tube, and these branches then reunite into a single tube of smaller cross section than the branches, so as to imitate roughly the relationships of arteries, capillaries and veins, the same quantity of liquid will flow through every total cross section of the system in unit time, and the velocity again will be inversely proportional to the total cross section area. In such an enlargement of the total cross section by branching the superficial contact between the liquid and the walls of the tubes becomes greater as the diameter of the branches becomes smaller, and the resistance therefore also becomes greater. Now increased resistance acts against the favorable influence which the mere widening of a current bed produces. Consequently the effect on the flow of the current produced by any particular branching of the bed will be the resultant of these two opposing factors.

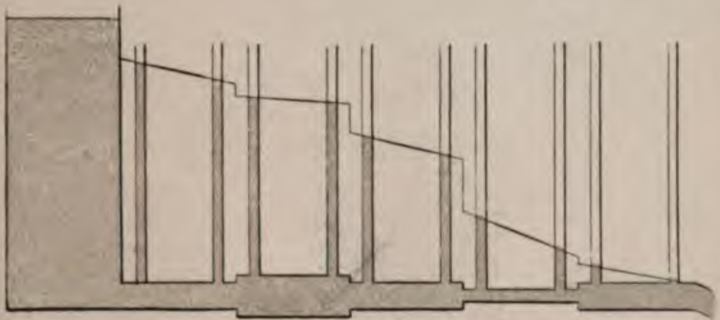

FIG. 73.—The flow of a liquid through a rigid tube of varying diameter.

§ 2. THE FLOW OF A LIQUID IN ELASTIC TUBES

The laws which apply to a *constant* current in rigid tubes holds also for tubes with elastic walls. But an important difference exists between rigid and elastic tubes, when the fluid is driven into them *intermittently*. We leave out of account here for the present wavelike movements in elastic tubes.

If a fluid be pumped rhythmically into one end of a *rigid* tube, it will flow out of the other end in jets of the same rhythm. But if we use an *elastic* tube for such an experiment, and if the resistance in the tube is sufficient and the rate of inflow rapid enough, the outflow may become continuous. This conversion of an intermittent to a constant flow is explained by the fact that the elastic wall of the tube is put on the stretch by the injecting force so that a part of the energy is stored in the wall. Then when the inflow ceases for a moment, the stretched wall exerts pressure on the contained fluid in consequence of which the latter flows during the pause between jets.

These conditions are realized in the vascular system. The blood is driven by the heart into the arteries in spurts; the arterial walls are elastic; the smaller arteries and capillaries present a high resistance. Consequently the arterial wall is stretched by the blood at every systole of the heart, and during diastole the *elastic recoil* of the wall drives the blood forward into the capillaries where its flow becomes constant.

The elasticity of the arteries *spares the heart* a considerable quantity of work. If they were rigid tubes, it would be necessary for the heart to drive the entire quantity of blood contained in them forward at once. But since they are elastic, the volume of blood discharged at each systole is accommodated by the temporary enlargement of the larger arteries and is then driven forward by the *force stored in their walls,* so that only a part of the column must be moved at the time of systole (E. H. Weber).

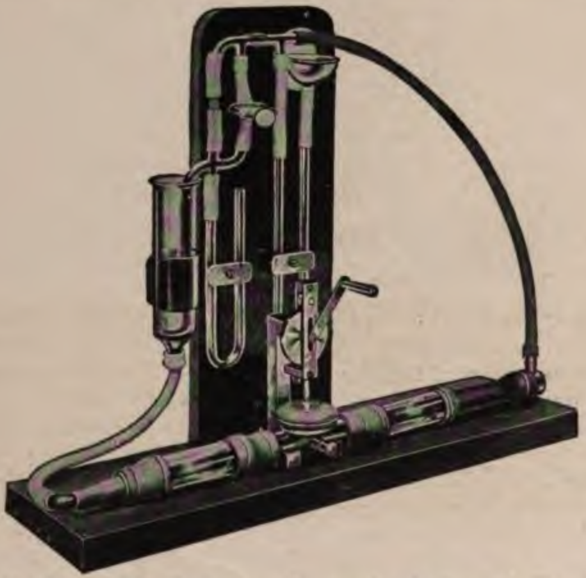

FIG. 74.—An artificial schema for illustration of some points in the mechanics of the circulation, after Porter. The schema consists of an "auricle" in the shape of a small cylindrical reservoir, shown at the left; a "ventricle" in the shape of a small rubber pump, the pressure within which is varied by means of a piston operated through an eccentric wheel which is rotated by a crank; a valve between the auricle and ventricle representing the atrio-ventricular valves; another beyond the ventricle representing the semilunar valves; tubes representing blood vessels; a set of "capillaries" in the shape of a section of porous cane where the "peripheral resistance" is high, and a side tube provided with a clamp by which the peripheral resistance can be lowered; and mercury manometers which exhibit the relative arterial and venous pressures.

The rhythmical feeding of the vessels has still another advantage. The blood corpuscles are given a kind of *to-and-fro* motion, which, as experiment has shown, materially facilitates the flow through the capillaries (Hamel).

§ 3. THE FLOW OF BLOOD IN THE ARTERIES

A. ELASTICITY OF THE ARTERIAL WALL

If a strip cut from an artery be stretched by adding to its load equal increments of weight, the amount of lengthening produced by each successive weight becomes steadily less the greater the total load. The coefficient of elasticity of the arterial wall therefore increases as the stretching force increases, so that the curve of elongation resembles an hyperbola (Wertheim).

As to the rate of *cubic distention* of the arteries caused by increasing internal pressures, which is a matter of much greater importance for understanding the circulation, the results of investigators differ widely. While Marey and others have found that the cubic enlargement runs the same course as the elongation of the strip cut from the wall, Roy asserts that this is the case only in arteries taken from animals and men who have suffered from some wasting disease, and finds that with perfectly sound arteries the increase in volume with equal increments of internal pressure rises at first up to a certain limit (variously given for the dog from 32 to 120 mm. Hg.), but with still higher internal pressure the distensibility falls (Fig. 75).

At any rate, it is certain that the cubic enlargement of the arteries beyond that given by a certain internal pressure, which as a rule is not higher than a medium, normal blood pressure, becomes less and less with equal increments of pressure. From which it follows that when the arterial blood pressure is already high, any steady increase in the quantity of blood discharge from the heart will cause a more than proportionate rise in the *blood pressure* and will correspondingly increase the work of the heart.

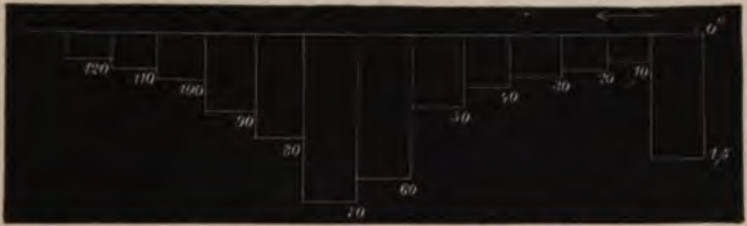

FIG. 75.—The cubic enlargement of the aorta of a rabbit, under a uniformly increasing internal pressure, after Roy.

From results thus far at hand it appears that with any given increase in pressure the arteries are distended relatively more the farther they are situated from the heart.

In the body arteries as well as veins are always on the stretch longitudinally, whatever the internal pressure; for the moment they are cut out of the body they at once retract, becoming shorter and thicker. It is always possible to find a stretching force which will give an exsected vessel the dimensions it would have if it were completely fixed *in situ*, when empty. This stretching force expressed as pressure in millimeters of Hg is looked upon by R. Fuchs as the measure of the longitudinal tension when there is no internal pressure; it amounts to from 50 to 90 mm. Hg. in the thoracic aorta of the dog, and is therefore below the mean blood pressure.

The *elasticity* of the arteries is perfect—i. e., if they be subjected to a high internal pressure, and the excessive pressure be then removed, they immediately return to the original volume.

Furthermore, the *resistance* of the arteries to high pressure is exceedingly great. The internal pressure necessary to rupture the carotid of the dog is four to eleven atmospheres, the carotid of man seven to eight atmospheres (mean). Since the maximum normal blood pressure in the carotid may be estimated at one-quarter atmosphere, we see that arteries can be ruptured only by a pressure twenty-eight to thirty-two times the normal. The resistance of the smaller arteries is still greater. This means that arteries can never be ruptured by excessive blood pressure, unless they have first been abnormally weakened (Hales, Gréhant and Quinquaud).

B. METHODS FOR THE DETERMINATION OF BLOOD PRESSURE

The *mercury manometer* is commonly used in determining arterial blood pressure, because it gives directly the absolute value of the pressure without any calculation. The *elastic manometer* also (page 9) finds wide application where it is desired to follow exactly the variations of pressure accompanying individual heart beats.

The Hg-manometer is not adapted for following rapid variations of pressure because of the *inertia of the Hg column*, which causes the maxima and minima corresponding to systole and diastole to be incorrectly reproduced. With a slow rhythm the maxima are too high, the minima too low; while with a quicker rhythm the maxima are too low, the minima too high.

But a tolerably satisfactory value of the *mean pressure* for a given time can be obtained by means of the Hg-manometer in the following way (v. Kries): In the figure given on page 8 the smaller oscillations on the curve represent individual heart beats, the larger represent pressure variations caused by the respiratory movements; the line *a b* is the line of no pressure, and the line T gives the time in seconds. When the mercury moves up the free limb of the manometer, it naturally falls just as much in the other limb (Fig. 3). If we neglect the error due to inertia of the Hg. column, the blood pressure at any instant is therefore twice the distance of the curve from the line of no pressure. Hence, in order to determine the mean blood pressure—e. g., during the period *a* to *b*, vertical lines are drawn from *a* and *b* to the curve, then the surface *a b d c*, is measured in square millimeters and is divided by the line *a b*. The quotient is the height of a rectangle of the same surface as *a b d c*, and with a base *a b*. *This height doubled is the mean pressure in millimeters of mercury.*

If the pressure curve presents no very great variations but runs along with perfectly regular oscillations as in Fig. 8 the mean pressure can be determined by simply measuring the highest and lowest points during the period, and doubling the mean of these two.

The mode of connection of the cannula with the artery must be borne in mind in interpreting the pressure obtained. If a T-cannula be used, and the unpaired limb be connected with a manometer, so that the current in the artery is not interrupted, the manometer records the lateral pressure of the blood in this particular artery at the place where the cannula is inserted. But as a rule it is more convenient to make the cannula terminal to the central end of the artery, so that the manometer records the lateral pressure of the larger artery of which the one used is a branch. Thus a cannula in the central end of the carotid gives the *lateral pressure* of the blood in the aorta.

Several methods, which proceed upon the principle of finding the pressure necessary to stop the blood flow in the artery investigated, have been devised for determining the *blood pressure in man.*

The *sphygmomanometer* of v. Basch consists of a button or plunger, bound to a metal manometer by means of a rubber tube. The button is placed over some superficial artery (preferably one that is supported on a solid substratum—

e. g., the radial), and pressure is applied until no pulse can be felt by the finger placed peripherally to the instrument. The pressure which the manometer now shows is the desired value. This instrument appears to be incapable of giving an absolute value of sufficient accuracy, although it has proved admirably fitted for the determination of *variations in pressure* in the same person, provided neither too little nor too much time is covered by such variations.

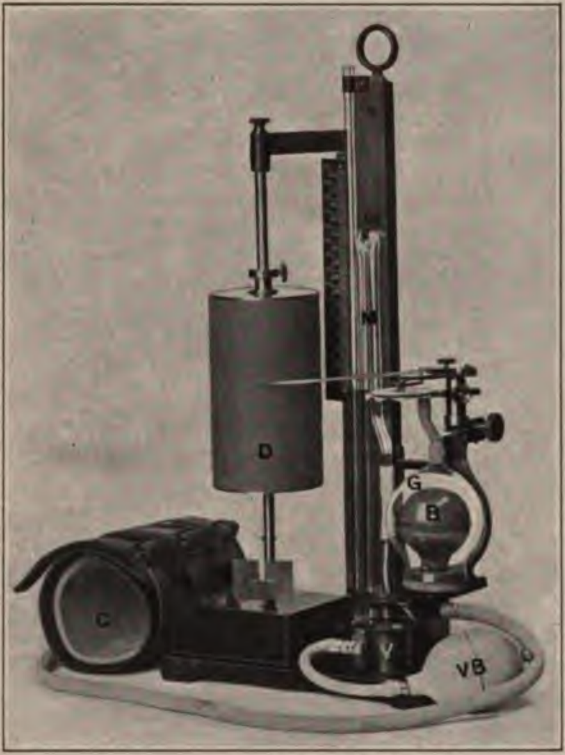

FIG. 76.—Erlanger's apparatus for determination of the blood pressure in man. The apparatus is provided with a pneumatic cuff, *C*, which consists of an inside rubber bag and an outside leather band. The whole cuff can be buckled around the arm above the elbow. The air cavity within the rubber bag of the cuff communicates through a thick-walled rubber tube and a four-way connection, ╪ with the three other essential parts of the apparatus, namely: (1) *downward*, with the valved bulb, *V B*, by means of which air can be forced into the cuff and can thus be made to compress the arm; (2) *to the left*, with the mercury manometer, *M*, from which the amount of pressure applied to the arm can be read directly in *mm* of *Hg;* and (3) *upward*, with the distensible bag, *B*, inside the glass chamber, *G*. This bag, last mentioned, responds to fluctuations of pressure inside the rubber bag of the arm, which are due to vibrations of the arterial wall, and the tambour at the top records such vibrations on the drum, *D*.

Other authors compress a section of a whole limb by means of a suitably constructed pneumatic cuff, and measure the pressure inside the cuff at which the pulse in some distal artery disappears or reappears. As H. v. Recklinghausen has shown, one must choose for this purpose a cuff of *considerable breadth*, for otherwise a portion of the pressure is consumed by the neighboring soft parts and one obtains too high a value. The broader the cuff, the more is this disadvantage obviated. With a breadth of about 15 cm. v. Recklinghausen observed in eight trials a variation of only 3 mm. Hg. in the blood pressure determined in the brachial and the femoral arteries at the same time. (In animal experiments the pressure in these two is in general found to be the same.) Such a method therefore gives very satisfactory results, as it is also much more easily manipulated than other methods thus far devised for this purpose.

[With Erlanger's apparatus (Fig. 76) it is possible also to determine the maximum systolic and minimum diastolic pressures. To determine the former the arm is compressed until no pulse can be felt in the radial artery. Even at this time the tambour of the instrument shows vibrations due to pulsations in the central stump of the artery; but if the air pressure on the arm be now lowered gradually by means of an escape valve (V in the Figure) these vibrations will suddenly become larger. The pressure which the manometer shows when this takes place is the pressure which the pulse wave can just overcome and is, therefore, the *maximum systolic* pressure. If the pressure be lowered still further the vibrations shown by the lever of the tambour will become still larger until a point is reached at which they begin to decrease. The pressure at which the arterial wall makes the widest fluctuations, and the lever therefore its largest vibrations, is the *minimum diastolic* pressure.—Ed.]

C. HEIGHT OF THE BLOOD PRESSURE

Since the *normal blood pressure* in the aortæ of different mammals shows but relatively slight differences, we can form an approximate picture of the blood pressure in man from the numerous determinations made directly upon different species of animals. The normal pressure in the dog is 130–180 mm. Hg., in the rabbit 80–120, in the horse 150–200. We may say, therefore, that the *mean normal blood pressure in man* varies between 100 and 200 mm. Hg., and if we wish to use a single figure we may assume that 150 mm. is the most probable value.

We are not, however, to regard the blood pressure as constant; on the contrary very considerable variations make their appearance on slight provocation. We have, therefore, to study the *factors upon which the blood pressure depends.*

These are essentially three: the energy of the heart, the resistance in the arteries, and the total volume of the blood.

1. *The Energy of the Heart.*—The quantity of blood which the heart expels in a given time may be taken as a *measure of its energy.* If, other things being equal, the quantity expelled in a given time decreases, the blood pressure falls as is the case for example upon stimulation of the vagus (Figs. 77–79. If, on the other hand, the decrease in pulse rate is only slight, and is compensated by a larger pulse volume (cf. page 189), the mean blood pressure falls only a little or not at all (Fig. 77).

The quantity of blood expelled from the heart may decrease also without a fall in the frequency of heart beats (cf. page 188), in which case of course the blood pressure falls.

On the other hand the energy of the heart may increase without any change in frequency of the pulse (cf. page 192), and a rise in pressure results.

When the heart is accelerated by division of both vagi, or by stimulation of the accelerator nerves, it may or may not expel more blood in a given time. If it does, the blood pressure increases (supposing that the caliber of the vessels has not changed); if not, the pressure remains the same. For a quicker rate does not necessarily imply greater energy of the heart beat, and so does not of necessity produce a greater output. Now it is evident that unless the total output in a unit time is increased, the quantity of blood coming back to the heart between two systoles is less with a rapid pulse than with a slow one, or, in other words, the pulse volume is less. Hence, the blood pressure following acceleration will depend upon the reciprocal relation between the increase of pulse rate and the decrease of pulse volume.

Direct investigations of this subject have resulted in showing that *no general law* can be formulated. If a large quantity of blood is found in the great veins, and is only waiting an opportunity to get into the heart, and if the resistance in the arterial system is sufficiently high, acceleration may produce a considerable increase in blood pressure. If these conditions are not fulfilled, the increased frequency will occasion no rise in pressure worth mentioning.

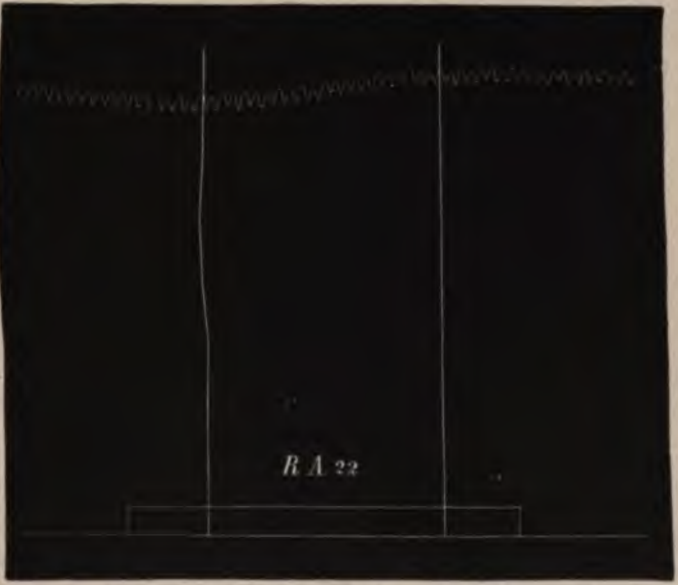

FIG. 77.—Blood pressure curve, showing a slight fall under feeble stimulation of the vagus. To be read from right to left. The time of stimulation is indicated by the two vertical lines. |‾‾‾‾‾‾‾| = ten seconds.

2. *Resistance in the Arteries.*—It is evident that with a given heart energy, if the resistance in the vessels decreases, the pressure also must decrease. If the resistance increases the pressure also must increase.

A fall in pressure in consequence of *diminished resistance* occurs, if the vessels in a large vascular region lose their tonus. Not only the arteries, but the veins as well are to be considered as taking a part in this; for the latter possess a certain tonus with the disappearance of which they are considerably dilated and so can contain more blood than usual. Hence the blood stagnates in the veins, and its flow to the heart is lessened considerably. The fall in blood pressure, therefore, is occasioned not only by the diminished resistance but also by the deficient flow to the heart.

The *resistance in the vessels is increased* either by constriction in a large vascular area, or by compression of a large arterial stem, for example the abdominal aorta. In the first case the blood flow to the heart is at the same time augmented, since the blood contained in the vessels is driven forward by their contraction. It is possible therefore that a larger quantity of blood will be expelled by the heart under these circumstances.

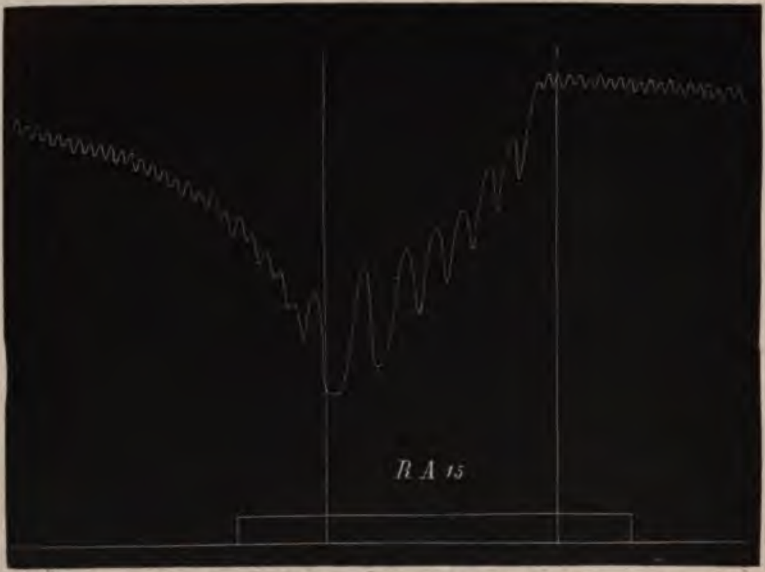

FIG. 78.—Blood pressure curve, showing a pronounced fall due to slowing of the heart, as the result of vagus stimulation of medium intensity. To be read from right to left. The time of stimulation is indicated by the two vertical lines. |‾‾‾‾‾‾| = ten seconds.

It might be supposed that by compression of the vessels the pressure could be forced up indefinitely. But this is not the case. The reflex mediated by the depressor nerve comes into play, so that either the vessels are dilated or the heart beats are retarded. But even if this reflex fails, there is an upper limit to the blood pressure beyond which it cannot pass. The *activity of the heart is not unlimited,* and we have good reason, based on many observations, for asserting that with a high resistance in the vessels the quantity of blood expelled in a given time actually diminishes.

3. *Quantity of Blood.*—Investigations on the influence of the blood volume go to show that when the vessels are overfilled the blood pressure does not exceed the normal physiological limits, and that when the vessels contain less than the normal quantity mechanisms are at hand for the purpose of maintaining the blood pressure at its normal height.

In what follows we shall consider first the results of adding to the normal quantity of fluid in the vessels. Let us suppose that blood or some other harmless fluid is *transfused* into the veins of an animal. The transfused fluid does not all go to the heart at once; a considerable part of it remains in the *central veins*, which thus become overfilled; and in the *liver*, which after the transfusion of a large quantity may become almost as hard as a board.

Furthermore, the entire quantity of transfused fluid does not remain in the vascular system, for the vessels relieve themselves by *transudation*. The nature of the fluid has much to do with the amount transuded. By means of blood counts it has been found, for example, that after transfusion of *blood*, about half the quantity transfused remains in the vessels at the end of the first day; while if *distilled water* is used in transfusion the blood quickly recovers its normal constitution (Worm-Müller, Regéczy).

Along with transudation the *secretory activity* of the glands increases and this coöperates to diminish the quantity of fluid in the vessels. Particularly is this true of the mucous membrane of the intestine and of the kidneys. If a NaCl solution be transfused not too rapidly into a vein, after some time transfusion and secretion of urine *exactly balance* each other (Dastre and Loye).

Thus by transudation and secretion the quantity of fluid is gradually brought back to the normal. But this takes place as a rule rather slowly, and other factors meantime must step in to regulate the blood pressure. One such factor is *vasodilation*, by means of which the resistance in the vessels is lowered (Worm-Müller). Another is the activity of the heart. If transfusion be performed slowly enough, the heart is able to throw a correspondingly larger quantity of blood into the vessels and so to preserve the cardiac pressure within safe limits. But if the transfusion take place more rapidly, or if the total quantity transfused be very large, the heart may drive more blood into the vessels than before the transfusion but not enough to prevent *stasis of blood in the heart*. Finally,

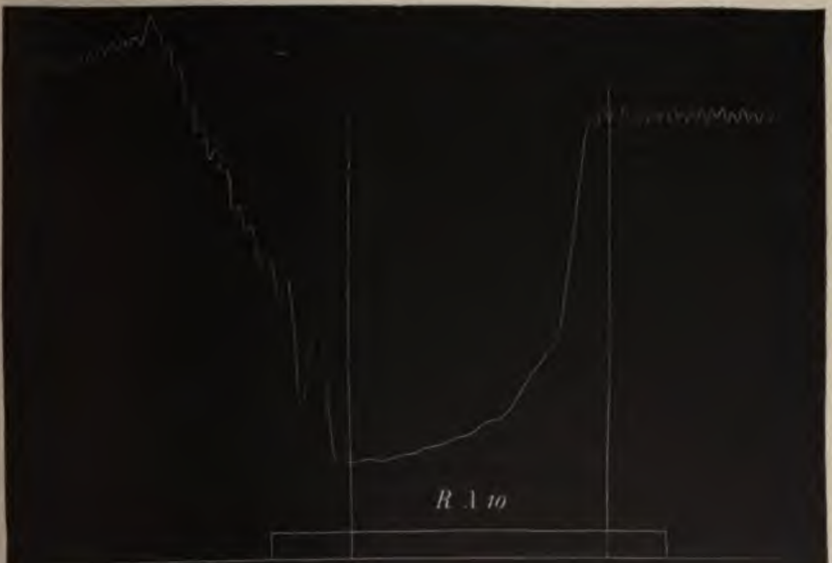

FIG. 79.—Blood pressure curve, showing a sudden fall due to stoppage of the heart, as the result of strong stimulation of the vagus. The time of stimulation indicated by the two vertical lines. ⌈ ⌉ = ten seconds.

the quantity transfused becomes so great that sooner or later the demands upon the heart are excessive, and the arterial blood pressure falls in spite of the abnormally large quantity of fluid in the vessels. One sometimes meets with cases where the heart works powerfully enough during the transfusion to overcome the increased quantity of blood, but later in the course of the experiment, after transfusion has ceased, symptoms of acute fatigue suddenly appear. In such cases the heart may be relieved and death averted by withdrawing a sufficient quantity of blood from the vessels.

We have in the circumstances mentioned above the explanation of heart weakness which sometimes follows ingestion of very large quantities of fluid by way of the stomach.

The reverse processes take place in *bloodletting*. The heart empties itself as completely as possible and drives the greatest possible quantity of blood into the vessels; the vessels contract and thereby present a high resistance to the blood stream; the kidneys, salivary glands and probably all the other glands diminish their secretions, and there occurs an increased passage of fluid from the lymph to the blood vessels.

By the coöperation of these factors the *blood pressure* under normal circumstances varies in general *within rather narrow limits,* notwithstanding the many influences which tend to change it in both directions. And yet, in order to produce significant variations in the pressure artificially it is often necessary to use only very weak stimulation. In fact, the stimulus may be so slight that at times one is wholly at a loss to make out the cause of the sudden increase or decrease in pressure which results. More on this subject will be found under the discussion of vasomotor nerves.

By means of an instrument constructed on the principle of the Basch Sphygmomanometer and applied to the radial artery of man, the blood pressure in the sitting or reclining position was found by Hill and Barnard to be 100–108 mm. Hg. It rose to 120, 130 or 140 mm. under various influences such as bodily movements, but sank again very rapidly toward the value for rest when the movements ceased. The blood pressure is raised also by a cold bath, but is depressed by a warm one (Edgecombe and Bain).

Blood pressure in the large arteries is not much higher than in those of smaller caliber, and decreases only slightly therefore with the distance from the heart. Especially is this true of diastolic pressure, whereas differences of systolic[1] pressure are greater. The cause of this slow fall in pressure in the arterial system is purely hydrodynamic in nature. The resistance against which the blood pushes in the larger arteries is small in comparison with that to which it is subjected in the smallest. The consequence is that the

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[[1] From numerous comparative observations made on dogs, Dawson concludes that "in considering variations in the systolic pressure, it is absolutely essential to distinguish between end pressures obtained from the *branches* of the main arterial trunk and those obtained from the *main trunk itself*. In the former case the systolic pressure shows a steady and considerable falling off which becomes apparent in end pressures taken, for example, in the thyroid arteries, in branches arising from the axillary and in branches from the lower part of the aortico-femoral trunk. When, however, the systolic end pressure is taken in the main arterial trunk, it is found that this pressure either remains high (axillary and brachial) or *may even greatly exceed* the corresponding lateral pressures in the aorta (iliac and femoral)."—Ed.]

driving power is not consumed rapidly until the smallest arteries are reached, and hence the fall in pressure in the large and medium sized arteries is only relatively small (cf. page 222).

D. VELOCITY OF THE BLOOD IN THE ARTERIES

There are two ways of determining the velocity of the blood in the arteries, according as one wishes to obtain the mean velocity in unit time, or the variations in speed which take place during a single heart beat.

The velocity can only be determined by placing the necessary apparatus directly in the path of the blood without interrupting its flow. Several forms of apparatus have been constructed for this purpose, the best known of which is Ludwig's *Stromuhr* or "current clock" (Fig. 80). It consists of two glass bulbs of equal size (A, B) which communicate directly with each other by means of the U-shaped tube above. By means of the opening at the top oil is placed in one bulb, A, and salt solution in the other, B, and the opening is then closed. The two fluids are in contact with each other above. The tube A is now connected with the central end and the tube B with the peripheral end of an artery. When the arteries are unclamped the blood flows into A and drives the contained oil over into B, the salt solution meantime being forced into the peripheral end of the artery. When the blood has completely filled the bulb A, the two bulbs are reversed, so that the blood flows now into B, displacing the oil once more and driving the blood from A into the peripheral end of the artery. The capacity of the bulbs being known, by counting the number of reversals necessary one

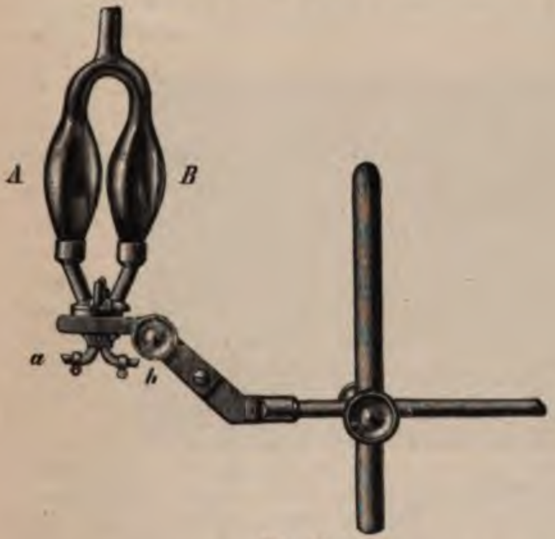

Fig. 80.

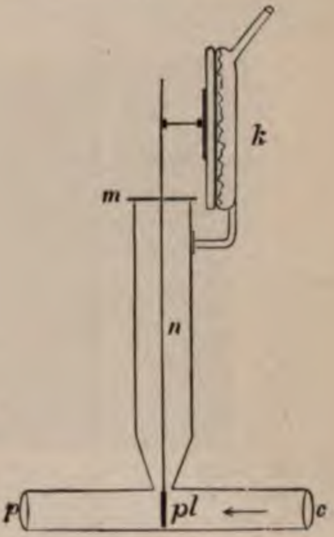

Fig. 81.

Fig. 80.—Ludwig's *Stromuhr* or "current clock."

Fig. 81.—Chauveau's hæmadromograph with air transmission. *n*, the needle; *pl*, small plate on the pendulum; *k*, a tambour influenced by the strokes of the pendulum. The blood flows in the direction of the arrow. *m*, a hard-rubber membrane which serves as a lid for the vertical tube and as a fulcrum for the pendulum.

can calculate the volume of blood which flows through the artery in a certain time. Registering current clocks have been devised by Ludwig and Hürthle.

In order to determine the variations of speed accompanying a single heart beat, Vierordt employed a hydrometric pendulum. If a pendulum be hung in a current of fluid, the length of its swing will depend on the linear velocity of the current, and on a small scale it will reproduce correctly all the variations of speed. Chauveau connected this pendulum with a writing tambour and by this means registered directly the variations in speed, and after graduating the instrument, determined their absolute values (Fig. 81).

The following results may be mentioned. The *amount of blood expelled per second* by the left heart of a rabbit (of 1.59 kg. body weight) into the aorta is on the average 1.35 c.c. The extremes in a series of fourteen experiments were 0.91 and 3.76 c.c., the mean was 2.10 c.c. The mean linear velocity, calculated from the diameter of the cannula tied into the aorta was 128 mm. per second (extremes 72 and 340 mm.).

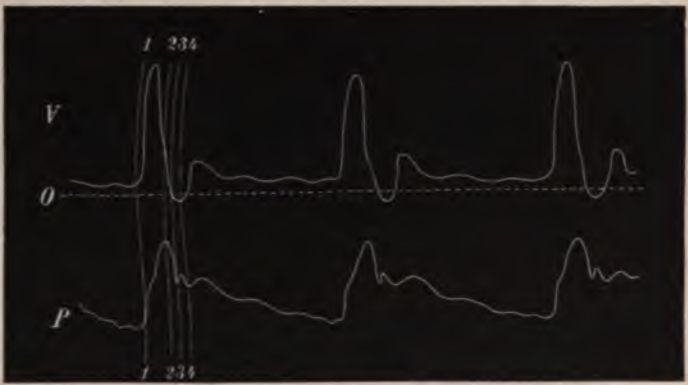

FIG. 82.—Velocity curve *V* and pressure curve *P*, carotid of the horse, after Lortet. The lines 1, 2, 3, 4 give the corresponding points on the two curves. At 1 the blood is forced into the aorta; between 3 and 4 the semilunar valves are closed.

During *systole* it is evident that the *velocity is greater* than during *diastole* (cf. Fig. 82). In the carotid of the horse Lortet found 520 mm. per second in systole and 150 mm. per second in diastole. At the end of diastole the velocity in the peripheral arteries is greater than in the central; while at the beginning of systole it increases considerably in the central and only slightly in the peripheral.

In dogs with a mean body weight of about 14 kg. Tschuewsky found for the velocity in the carotid and crural arteries the values summarized in the following table:

Body wt.	Artery.	Vol. per second.	Lin. Veloc. per second.	Diam. of artery.	Blood pressure.	Remarks.
13.7 kg.	Crural.	0.63 c c.	128 mm.	2.5 mm.	77 mm.Hg.	Nerves uninj.
14.6 "	Crural.	1.69 "	275 "	2.8 "	88 " "	Nerves cut.
14.1 "	Carotid.	1.95 "	241 "	3.3 "	93 " "	Nerves uninj.

Thus the velocity is seen to increase considerably after section of the nerves controlling the arteries, and to be considerably greater in the carotid than in the crural. One cannot therefore draw conclusions as to the velocity in one artery from determinations made for another.

When one carotid is *ligated* the velocity in the other increases materially, as for example in two dogs of 13.7 kg. mean body weight, on the average from 2.63 c.c. and 266 mm. per second to 3.47 c.c. and 350 mm. per second.

Likewise the velocity increases considerably after a temporary *compression* of the artery, as for example in the crural (dog 13.2 kg.) from 0.783 c.c. and 149 mm. per second before compression to 1.252 c.c. and 255 mm. after. The pressure in both cases was 89 mm. Hg.

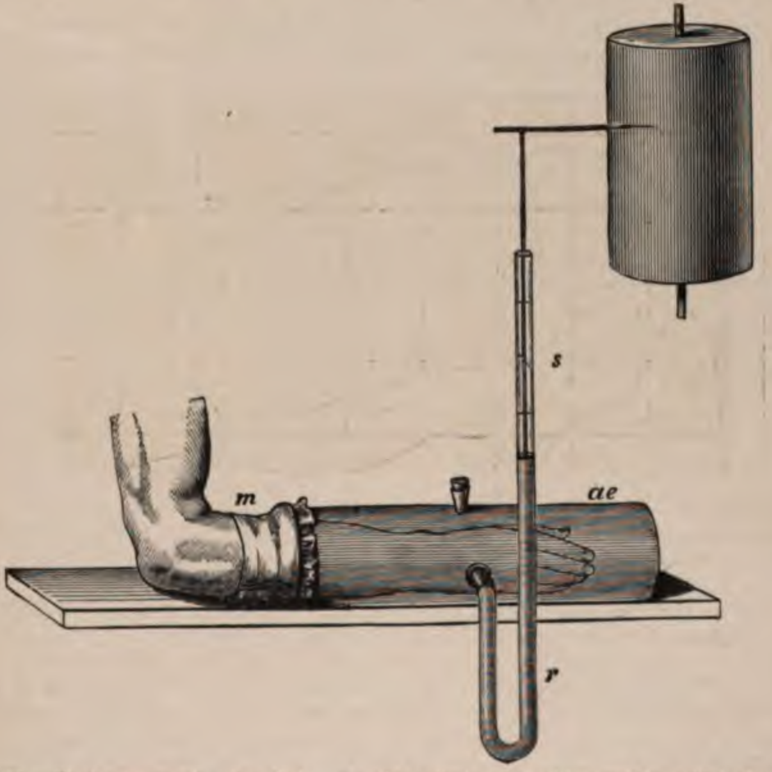

FIG. 83.—Plethysmograph, after Fick. *a e*, the cylinder; *m*, rubber cuff by which the cylinder is made to fit air-tight over the arm; *r s*, recording monometer.

On account of the dilatation taking place in the arterioles of an organ during its *activity*, the velocity is increased considerably in the arteries supplying it. Thus Chauveau observed that the velocity in the carotid during mastication rose to five or six times its usual height.

Finally, when the vessels are dilated as a result of section of the spinal cord, the velocity increases during systole, but is extremely small during diastole.

In man the *variations* of *velocity* in the peripheral arteries can be estimated, but no absolute value can be obtained.

To understand the principle of the method employed, we must bear firmly in mind that the blood in the peripheral veins flows continuously, exhibiting as a rule no variation due to the heart beats or to the respiratory movements.

If a part of the body—for example, an arm—be placed in an air-tight cylinder the cavity of which is connected with a suitable recording device, a Marey tambour or manometer (plethysmograph, Fig. 83), a curve is traced in which the separate heart beats appear clearly marked. The variations thus recorded are caused by the variations in the volume of the arm, and the so-called *plethysmographic curve* (Fig. 84) is therefore a volumetric curve.

Since the return flow in the veins is constant, the variations are produced by *fluctuations in the arterial flow*. When the curve rises the arterial inflow is greater than the venous outflow; when it sinks, the inflow is less than the outflow, and when the curve runs horizontally inflow and outflow balance each other.

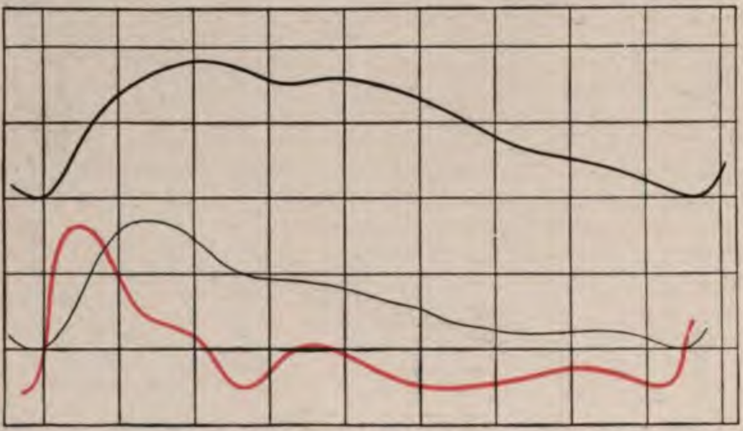

FIG. 84.—Plethysmographic curve (the upper black line). Pulse curve (the lower black line), and velocity curve (red) in man, after Fick. To be read from left to right.

It is clear however that the *volume changes* of the arm will follow more quickly the more rapid is the flow of blood to the arm. Thus if we estimate the steepness of the changes in different sections of the curve, we can construct a velocity curve from the volume curve (Fick). In Fig. 84 the red line represents the velocity curve derived from the volume curve (the upper line). Its similarity to the curve recorded by means of the hydrometric pendulum, and pictured in Fig. 82, is unmistakable. In both we have, after a sharp rise, a fall, upon which follows an increase in velocity again. The latter coincides in time with the so-called dicrotic wave of the pulse curve (cf. below).

§ 4. THE ARTERIAL PULSE

A. THE MOVEMENT OF WAVES IN ELASTIC TUBES

Imagine an elastic tube, filled and distended with water, to be divided by fixed lines into the segments *a*, *b*, *c*, *d*, *e*, *f*, *g*, *h*, *i* (Fig. 85). The piston, we will suppose, has driven the water from the rigid tube (k) into the distensible tube (ai), with a velocity at first increasing and then diminishing, and has thus dilated the tube, while the water contained in the different segments has been given a velocity indicated by the number of dotted arrows in each. If then the ring-shaped sections of the wall inclosing the segments exert a pressure upon the contained liquid, the amount of which is represented by the solid-line arrows, it is evident that the particles of water contained in the segments e, f, g, h, will be accelerated in the direction i (since they were already moving in this direction). On the other hand the particles contained in the segments d, c, b, a will be retarded in their movement, since the pressure indicated by the solid arrows is exerted in the direction of k. For this reason the liquid in a comes to rest within the next few moments, and the distended wall of this segment returns to its original diameter. During the same time, the water in segment i, which until now had not been moved, is pushed forward and its wall is distended. Thus the *wave is propagated* from one segment to another in the direction of the dotted arrows (E. H. Weber). The water presses upon the wall of the tube, the wall in turn presses upon the water, and the wave spreads with a velocity (V), which is inversely proportional to the square root of the specific gravity (Δ) of the liquid, and of the internal diameter of the tube (d); directly proportional to the square root of the wall's thickness (a) and of its elastic coefficient (e) (Moens). The law is expressed by the following formula $V = k\sqrt{\frac{gea}{\Delta d}}$ in which k is a constant and g is the acceleration of gravitation.

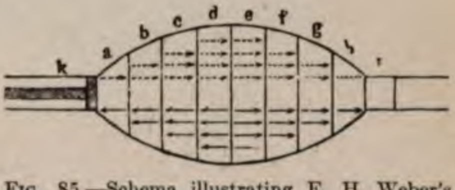

FIG. 85.—Schema illustrating E. H. Weber's theory of the pulse.

The wave is changed in form more or less in its propagation through the tube by the *resistance due to friction.* Its height is less and its length greater than if there were no friction.

The moment an elastic tube, already filled with an incompressible liquid, receives an extra quantity, a *wave of increased pressure* is started, and is propagated along the tube. If the flow be maintained for a time, the pressure keeps a certain level for each point along the tube, the value of which is determined by the same laws that apply to the flow of a liquid in rigid tubes (cf. page 198).

If one end of an elastic tube filled and distended with water be suddenly relaxed by removal of a quantity of water, a fall in pressure is propagated in the form of a *negative wave* to the other end of the tube. Likewise if a regular current flowing through an open elastic tube be suddenly checked, a negative wave is set up which travels in the direction of the current.

Besides, if the tube be not so long that waves thus set up entirely disappear, as the result of friction, new ones will arise by *reflection* from the end of the tube, which will materially affect the wave movements. If the end of the tube where the reflection occurs be closed, the wave will be reflected with the same sign, a positive wave as a new positive wave, a negative wave as a new negative one. If the end of the tube be open, the wave will be reflected with its sign reversed, a negative as a positive and a positive as a negative. The same wave may by repeated reflection run the length of the tube several times. If the end of the tube be only partially closed, every primary positive wave will be transformed into a reflected one which is partly positive and partly negative.

Since both these reflected waves travel through the tube with the same velocity and naturally interfere with each other, it depends on the degree of constriction whether the algebraic sum of the two will be a positive or a negative wave, or will be *nil* (Grashey).

If from a simple tube A, a side branch B be given off, every wave which runs through A will traverse also the branch B; and, it matters not whether the wave arises in the wide or in the narrow tube, it will traverse both. This statement holds also for a complex system of tubes, and we may say in general that when a wave starts from any point of a branching system of vessels, it is *propagated to all the branches.*

Reflection takes place in such a system at every dividing place. But if the velocity with which the waves are propagated changes at any point in the same proportion as the cross section changes, no reflection occurs (v. Kries).

All the conditions for the origin of primary and reflected waves and of interference are found in the arterial system. The difficulty consists only in isolating from among the theoretically possible movements, those which cause the peculiarities of the arterial pulse.

B. THE PULSE

The ancient physicians distinguished in the pulse a number of different qualities, which can be reduced to four: *frequency, size, velocity* and *hardness.*

With respect to frequency, the rapidly repeated pulse (*pulsus frequens*) is to be distinguished from the less frequent (*rarus*). With respect to size we have the large (*magnus*) in which the expansion of the artery under the finger is large, and the small pulse (*parvus*) in which the expansion is small. With respect to velocity the quick pulse (*celer*) in which the artery presses against the finger suddenly and disappears suddenly, can be distinguished from the sluggish pulse (*tardus*) in which the impact is more prolonged. And with respect to hardness, the pulse (*durus*) which can be compressed with difficulty, can be distinguished from the one (*mollis*) which can be easily obliterated by pressure. On the basis of these four fundamental qualities a series of other qualities can be named, but we shall not discuss them further.

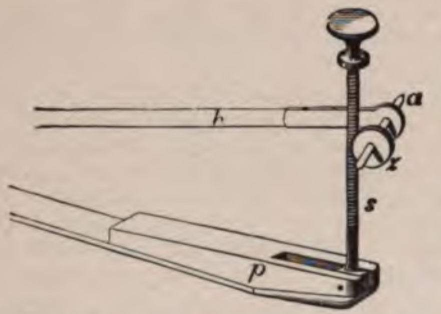

Fig. 86.—The spring of Marey's sphygmograph.

Knowledge of the pulse has made rapid progress since E. H. Weber gave it a mechanical explanation (1850) and Vierordt showed that it could be graphically recorded (1855). The first pulse recorder (*sphygmograph*) to give correct pulse curves was constructed somewhat later (1860) by Marey.

The most important part of the sphygmograph (Fig. 86) is the steel spring (p) with a contact surface to be placed over the artery. This spring responds to the movements of the artery and transmits the movements to the writing lever, which magnifies and records them on a writing surface driven by a small clockwork. The movements of the spring are transmitted to the lever by means of the screw s, jointed to the contact surface, and the tension of the spring can be regulated by means of another screw. The whole apparatus is fastened by means of a band to the lower end of the forearm (Fig. 87). Many modifications of this instrument are in use.

The method of *air transmission* is often used also, especially when it is desired to register the pulse curves of two or more arteries, or the pulse curve and cardiogram, at the same time. A receiving tambour of about the same construction as that described for the apex beat is fastened over the artery and is connected in the usual way with the recording tambour (cf. Fig. 10, page 12).

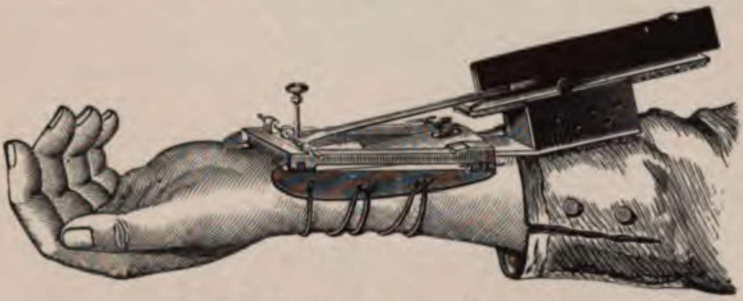

FIG. 87.—Marey's sphygmograph as used.

The sphygmograph has *often been tested* and it has been found to give the pulse movements with surprising accuracy. It has been shown, for example, that it reproduces very exactly the waves, already known, by other means, to occur in an elastic tube (Mach); that the pulse curve has exactly the same appearance when the pulsations are recorded without magnification and where the inertia of the lever is thus reduced to a minimum (Marey); and that pulse curves having exactly the same form as those recorded by the sphygmograph, are obtained if a very small mirror is fastened to the skin over an artery, so that the light may be reflected on a wall.

But we must not suppose that every sphygmograph records pulse waves so perfectly. It often happens on the contrary that the instrument *distorts* the curve considerably. It is, therefore, necessary in every exact study of the pulse by the graphic method to assure oneself of the efficiency of the instrument and of the maximal speed permissible for the lever.

The *velocity of the pulse wave* is measured by taking at the same time pulse tracings from two arteries separated by some distance from each other. The velocity of propagation found in this way varies with different individuals, and with the same individual under different circumstances. In a healthy man it amounts to 7–10 m. per second. The velocity is greater, the greater the coefficient of elasticity. It increases therefore with a rise of blood pressure, for, as we have seen at page 201, the coefficient of elasticity of the arterial wall increases, at least within certain limits, as the internal pressure increases.

The length of the pulse wave λ is obtained from the formula $n\lambda = h$; or $\lambda = \frac{h}{n}$, where h is the velocity of transmission and n the rhythm. Since with each ventricular systole the blood is driven into the aorta for 0.2 of a second, the rhythm number is 5. With a velocity of 8 m. the length would be $\lambda = \frac{8}{5} = 1.6$ m. In a grown man the distance from the heart to the farthest arteries is just about equal to this wave length. Only the very longest arterial paths in the body, therefore, are long enough to include the entire length of a pulse wave; for the end of a wave enters the aorta only after the beginning of it has already reached the periphery.

Since the movements of the contact surface of the instrument are caused by fluctuations of pressure inside the artery, the *pulse curve* gives expression to the rise and fall of this pressure. But it does not represent the variations of arterial pressure exactly, for the arterial pressure is exerted not only against the contact surface but also against the arterial wall and the neighboring soft parts.

The sphygmograph is affected also by other movements than those of the blood in the arteries—e. g., by *changes of turgor* of that part of the body where it is applied. If the return flow of the blood from the veins is hindered, the entire series of curves in the sphygmogram rises because the swelling skin increases the tension of the spring. One dare not infer a rise of blood pressure, therefore, from such a rise in the series of curves.

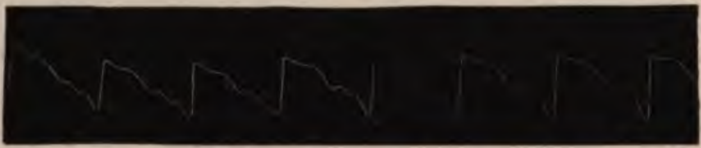

FIG. 88.—Radial pulse curve recorded with Marey's sphygmograph, after Langendorff. To be read from left to right.

When suitable apparatus is employed the pulse curve presents a *number of peculiarities,* some of which constantly recur more or less well marked, whatever the artery from which the curve is taken.

The pulse curve (Fig. 88, cf. also Fig. 11) begins with a rather *steep ascent* which corresponds to the positive wave caused by the inflow of blood into the aorta. This line usually reaches its highest point without interruption, whence begins immediately the descending limb of the curve. The latter shows several irregularities, one of which at least, the second mound, occurs in all pulse curves (Fig. 88). This mound is designated as the *dicrotic elevation.* That it is not an artifact has been shown by the above-mentioned tests to which the sphygmograph has been subjected.

The dicrotic elevation is without doubt a positive wave running in the centrifugal direction; but opinions differ as to the *way in which it arises.* Of the two hypotheses which at present are worthy of discussion, one accounts for the elevation by supposing that the primary pulse wave is reflected as a positive wave from the periphery of the arterial system. This reflected wave comes into the aorta, strikes against the closed semilunar valves, and is once more reflected without change of sign. The *second reflection* (that from the semilunar valves) is the cause of the dicrotic elevation (v. Kries, v. Frey).

According to the other hypothesis the dicrotic elevation arises in the following manner. When the cardiac contraction ceases, and the semilunar lves are no longer supported by the blood in the heart, or by their own muscular folds (cf. page 167), a negative wave starts from the root of the aorta running toward the periphery, and a portion of the aortic blood flows back toward the heart. When this returning blood strikes against the semilunar valves, which have just been closed, a *positive centrifugal wave* starts at the root of the aorta, producing the dicrotic elevation (Marey, Grashey *et al.*).

We cannot discuss here the principles underlying these two explanations. Both have eminent advocates and an agreement is not yet in sight.

However we conceive the dicrotic character to be produced, it is certain that waves reflected from the periphery of the arterial system have a very material influence on the *form of the pulse curve*. The reflected waves interfere with the direct ones; they spread to neighboring arteries where again they are propagated as direct waves, which in turn interfere with both the direct and reflected waves proper to these arteries, and so on. Thus a great variety of pulse tracings with a varying number of secondary and tertiary elevations on the pulse curve may be obtained.

Attempts have frequently been made to draw conclusions as to the *activity of the heart, the condition of the blood vessels, and the blood pressure* from the character of the pulse curve. This is possible to a certain extent, but must be done with great *caution*.

The pulse curve may give some *approximate information* as to the temporal course of events in the heart. The beginning of the pulse curve corresponds to the entrance of the blood wave into the arteries, and the beginning of the dicrotic elevation is synchronous with the beginning of a corresponding elevation on the cardiogram. Since this point appears at a slight interval after the closure of the semilunar valves (cf. page 175), the time elapsing between the beginning of the pulse curve and the dicrotic elevation is slightly greater than the time during which the left ventricle and the arteries are in open communication with each other.

It might be supposed also that a pulse curve of large amplitude would indicate a large pulse volume; but this is true only in a very limited sense, for the pulse curve of a given artery depends to so great a degree upon the tonus of this artery and upon the resistance in its peripheral branches that *no definite relation* between volume and size can be laid down.

Moreover, a large amplitude of the pulse curve is by no means significant of a high blood pressure, but at best signifies only that the fluctuation of pressure is great. But since we know that the variation of systolic pressure is within certain limits less with a high than with a low pressure, we might possibly say that under circumstances otherwise the same the greater amplitude means a lower blood pressure. But even this is not invariable. The degree of constriction of the artery under investigation has much to do with it.

Again the *height of the dicrotic elevation* has often been regarded as an index of the pressure, a greater elevation being produced with a low than with a high pressure. In many cases this is true. But there are exceptions, since the degree of dilatation of a particular arterial region may influence the production of any particular dicrotic pulse.

All of this shows how careful one must be in drawing conclusions from the pulse curve regarding the condition of the vascular system.

The pulse, as a rule, can be detected *only in the arteries.* This is explained by the fact that in any elastic tube a wave tends to be obliterated by friction. In an unbranched tube the length necessary for this obliteration would be very great, but in one composed of many branches like the vascular system, the obliteration is favored by every bifurcation, since thereby the total wall becomes greater and the active force of the wave is consumed the more rapidly. The wave is reflected also at every point where the vascular wall changes direction, and on this account it is consumed sooner than otherwise.

§ 5. FINAL SURVEY OF THE MOVEMENTS OF THE BLOOD IN THE ARTERIES

Now that we have learned the details of the blood flow in the arteries, it remains for us to reconstruct these details into a connected whole. We shall follow for this purpose the description of E. H. Weber.

Let us suppose that the heart consists of only one ventricle, also that to begin with the blood in all divisions of the vascular system is under the same pressure. When the ventricle contracts the atrio-ventricular valves close and prevent the blood from flowing backward. All the blood must therefore take the same direction into the arteries. If these were rigid tubes no blood could be pressed into them without at the same time setting in motion the entire column of blood in all its parts. In this case no wave would be produced, but only a stream of blood which would last as long as the contraction of the ventricle continued. But since the arteries are elastic tubes, propulsion of the different segments of the blood column takes place successively. The mass of blood discharged from the ventricle can find a place for itself only by distending a portion of the arterial system, and thus producing a positive wave of high pressure which spreads through the vessels.

If there were no semilunar valves, and if the ventricular contractions stopped immediately after the discharge of the blood, the distended arteries would at once drive a part of the blood back into the ventricle. But since this is prevented by the semilunar valves, the successive parts of the blood column are moved a little farther forward in the vascular system by each ventricular systole.

As soon as the heart relaxes at the end of systole and the atrio-ventricular valves are open, the blood flows from the veins into the heart and produces a negative wave which is propagated along the veins. The valves connected with the heart are so arranged that with the systole and diastole of the heart periodically alternating, positive waves pass out only along the arteries, negative waves only along the veins.

If the vascular system were composed of a single continuous tube of uniform diameter every wave would run through the entire system with great velocity, and would produce a state of equilibrium in the entire circuit before the next ventricular systole could follow. But because of the resistance in the smallest arteries, veins and capillaries, matters are quite otherwise. On account of the friction in the smaller vessels the blood cannot pass through as rapidly as would be necessary for the propagation of a positive wave all the way back to the heart. The wavelike movement is reflected, therefore, at the capillaries, etc., and under normal circumstances the pulse cannot be perceived in the veins.

Supposing now, as we have done, that the pressure is everywhere the same to begin with, then if the regular contractions of the heart were repeated rapidly enough, there would be an accumulation of blood in the arteries, for at each systole more blood would be thrown into the arteries than could be pressed through into the veins in the same time. At every diastole of the heart the total quantity of blood in the veins would be still further reduced, because more blood would pass from them into the heart than could come into them through the capillaries from the arteries. Thus the quantity of blood in the arteries would go on increasing, and the quantity in the veins would go on decreasing until the difference in pressure between the two would become so great that from one systole to another just as much blood was pressed through the capillaries as was being discharged by the heart into the arteries. Once this degree of difference in pressure between the two divisions of the vascular system had been reached, if the heart activity continued the same, the difference would become constant—i. e., the pressure in the arteries would be permanently greater than in the veins.

It is because of this constant *difference in pressure between arteries and veins* that the movement of the blood from the former to the latter takes place in a *steady stream.* For this reason also the blood continues to flow from arteries to veins for some time after the heart stops beating. Any sort of influence which changes either the resistance in the vessels or the energy of the heart, disturbs this stationary condition and a new equilibrium is established at a different level of arterial pressure. Every variation in pressure is in turn followed by a change of one kind or another in the character of the blood flow.

§ 6. THE FLOW OF BLOOD IN THE CAPILLARIES

The capillaries are unquestionably the *most important part of the vascular system.* The purpose of the circulation, which consists in supplying combustible materials and oxygen to the organs, and in relieving them of decomposition products, is accomplished in the capillaries. In them the blood is separated from the lymph by only a thin wall, consisting of a single layer of cells, through which the exchange of diffusible substances is readily carried on. The arteries and veins are only tubes conveying the blood to and from the capillaries: the latter constitute the real clearing-house of the vascular system.

Since oxygen is consumed in large quantities in the tissues, it is evidently of great importance that the blood should not flow too slowly through the capillaries. The high pressure which prevails in the arteries is *necessary in order to keep the blood flowing through the capillaries with sufficient speed.*

Whenever the pressure in the aorta falls, the pressure in the capillaries also falls. If an artery becomes constricted, the lateral pressure in this artery central to the place of constriction increases, but at the same time the pressure and velocity peripheral to that place, that is, in the capillaries, decreases.

Whenever, other things being equal, an artery is dilated, the lateral pressure in this artery may fall, but a larger amount of blood flows into the capillaries and as a result the pressure in them increases.

All the complicated mechanisms which help to regulate the blood pressure have for their immediate purpose the maintenance of a normal pressure in the aorta, in order that the blood may flow under normal pressure through the capillaries.

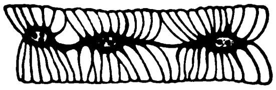

FIG. 89.—Branched contractile cells embracing wall of a capillary vessel in the hyaloid membrane of the frog's eye, after Rouget.

The total quantity of blood in the body is by no means sufficient to supply all the capillaries at once with as much blood as the organs require at their maximum activity. Fortunately all the organs are never at their maximum at the same time, so that their requirements vary. In fact the quantity of blood flowing through the capillaries varies incessantly. An organ upon which devolves an extra quantity of work receives for the time a greater supply of blood than if it were relatively inactive. The arteries belonging to the organ dilate, while the arteries which convey blood to the other organs at the same time constrict. By this means a fall in the aortic pressure is prevented and the blood flows *more copiously to the capillary system whose arteries have been enlarged.* Pressure and velocity in this region increase together.

The length of the capillaries is given as 0.4–0.7 mm. (in the liver as much as 1.1); their diameter is about 0.009 mm.

The capillary wall is composed of flattened cells which fit together by their edges. That they are capable of constricting in many places was first demonstrated by Stricker. Rouget and S. Mayer then showed that this constriction is brought about by contractile elements situated outside the basement membrane irely distinct from it. The nuclei of these cells are arranged parallel to the vessel and their cell substance is often divided into little t at right angles to the nucleus and embrace the capillary a barrel (Fig. 89). The contraction of these elements men of the vessel; at the same time fine longi-

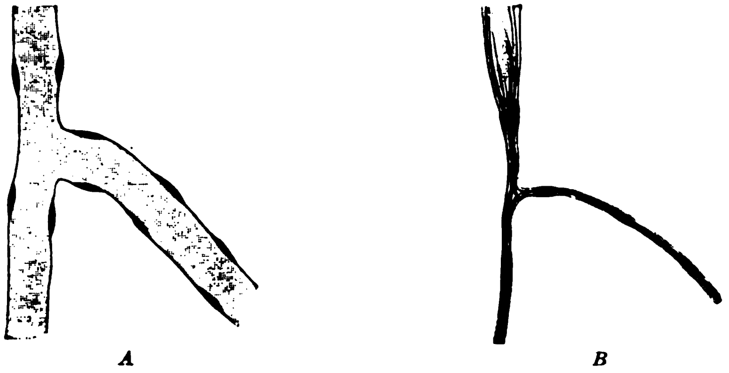

FIG. 90.—*A*, capillary when not stimulated; *B*, the same capillary stimulated. The lumen is entirely obliterated, after Steinach.

tudinal folds or wrinkles appear in the cell membrane, which increase in number, clearness and extent as the capillary wall draws together, and entirely disappear when the vessel dilates again (Fig. 90). However, certain individual capillaries or capillary tracts are quite exempt from this contraction (Steinach).

The most favorable object for the demonstration of these phenomena is the nictitating membrane of the frog. Quite similar results have been obtained also in other capillary systems of the frog and even of Mammals.

Capillaries are abundantly supplied with nerves, and Steinach has succeeded in producing a contraction of the capillaries in the frog's nictitating membrane by stimulation of the sympathetic.

Since the diameter of the capillaries may vary independently of the blood pressure, it follows with great probability that in virtue of their contractility the capillaries themselves participate to a considerable extent in the regulation of the blood supply to the different organs.

The blood in the capillaries flows in the following manner. If the capillary vessel is not so small that the blood corpuscles entirely fill it, the red corpuscles move along with their long diameters in the direction of the current, and keep to the center of the vessel, so that between them and the vascular wall a clear space is left filled with plasma. In this space are found numerous white blood corpuscles which sometimes come to rest there, sometimes roll along very slowly making frequent pauses. As a rule, the current in the capillaries is continuous. But there are exceptions to this rule. With sufficient dilatation of the small arteries in a given vascular region the blood stream in the capillaries may exhibit *rhythmical vibrations synchronous with the heart beats.* A continuous flow presupposes therefore that the blood in the small arteries meets with sufficient resistance to obliterate these pulsations.

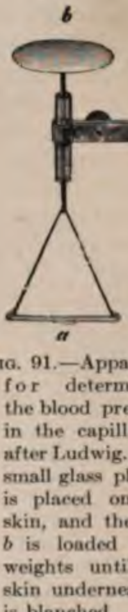

FIG. 91.—Apparatus for determining the blood pressure in the capillaries, after Ludwig. The small glass plate *a* is placed on the skin, and the pan *b* is loaded with weights until the skin underneath *a* is blanched.

In the field of the microscope the *velocity* of blood flow in the capillaries can be determined by simply observing the time consumed by a particular corpuscle in traversing a measured distance on the eyepiece micrometer. The velocity determined in this way is given as 0.5–0.8 mm. per second. These values however are maximal, for they relate to the current in the central part of the vessel. The mean velocity is somewhat less.

Attempts have been made to determine the *blood pressure* in the capillaries by measuring the pressure upon the outer surface of the skin or upon the gums of the teeth (Fig. 91), at which a distinct change in color appears. This is said to indicate that the most superficial capillaries are completely compressed. The limits of error of this method are rather wide, and the values obtained can only be regarded as bare approximations to the truth. This appears more clearly when we bear in mind that the pressure thus determined is not the total capillary pressure, for the lymph exerts an opposite pressure on the outer side of the capillary wall, and this depends upon the tension and the turgor of the skin.

The capillary pressure which one obtains when the effect of the hydrostatic pressure of the blood column is excluded—i. e., when the capillary region investigated lies at the same level as the heart, amounts to about 33 mm. of mercury (N. v. Kries, gums of the rabbit). Since the aortic pressure in the rabbit amounts to about 100–120 mm. Hg., the capillary pressure would be one-third to two-sevenths of the aortic pressure.

Poisseuille has given the following formula for the flow of a fluid through a horizontal capillary whose wall is wet by the fluid: $Q = \pi \frac{p_1 - p_2}{8\eta l} r^4 t$ where Q represents the volume of fluid flowing through the capillary in the time t, p_1 the hydraulic pressure at the beginning of the capillary, p_2 that at the end, l the length, and r the radius. η is the constant of internal friction If all the dimensions are given in millimeters and milligrams, η in milligrams is the retarding force of the friction taking effect upon one square millimeter of surface, when the difference in velocity between two adjacent layers of the fluid one millimeter apart is 1 mm. per second, the change in velocity being uniform. The greater the value of η (i. e., the more viscous is the fluid), the less becomes the volume of fluid which will flow through the tube in unit time.

It has been shown by B. Lewy that this law is true also for the blood. At a temperature of 36°–40° C. he found the mean value of η to be 0.00025 (swine, sheep), whereas the corresponding value for distilled water is 0.00007. The internal friction of defibrinated blood is thus on the average 3.5 times as great as distilled water. The internal friction of normal blood is somewhat greater. According to the researches of Hürthle, at 37° C. it amounts to 4.7 for the dog, 4.3 for the cat, 3.3 for the rabbit, that of distilled water being taken as 1. Moreover the internal friction of blood varies considerably under different circumstances. It decreases after bloodletting; it is smaller in starvation than after feeding; and in the dog it reaches its highest value after feeding meat (Burton-Opitz). Relying upon data concerning the internal friction of defibrinated blood, and under certain assumptions as to the length, breadth, etc., in different parts of the vascular system, B. Lewy has calculated the fall in pressure in the capillaries and has found it equal to 20–60 mm., or by using the highest value of η (0.00068) observed by him, equal to 150 mm. of blood.[1] At the most, therefore, about one-fourteenth part of the entire blood pressure is consumed in the capillaries themselves. From which it follows that it is not the capillaries which constitute the chief resistance to the blood stream, but rather the smaller arterioles central to them.

Campbell also has reached the same view from altogether different considerations. Among other things he emphasizes the point that if the resistance in the capillaries were very great, so that the pressure at the beginning of a capillary were much higher than at its end, the very thin capillaries would be funnel shaped with the wide opening directed toward the arteries, which, as we know, is not the case.

With the help of Poisseuille's formula, and on the basis of data already at hand for the internal friction of the blood, for the quantity of blood flowing through the aorta, and for the pressure therein, Hürthle has calculated the absolute resistance in the aortic path (rabbit). As is evident from the formula, this is expressed as the length of a tube through which just as much blood would flow in unit time as flows through the animal body. According to this calculation the resistance is equal to that of a cylindrical tube with the diameter of the aorta and with a length of 296 m. It need scarcely be remarked that this value relates only to a special case, and that it is adduced here only for the purpose of giving an approximate idea of the amount of resistance in the vascular system.

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[1] Approximately 11 mm. Hg.

§ 7. THE FLOW OF BLOOD IN THE VEINS

A. PRESSURE AND VELOCITY

The *cubic distention* of a vein to internal pressures increasing by equal increments is exactly like its longitudinal distention to loads increasing by equal increments—i. e., it becomes less the higher the total pressure becomes (Fig. 92). The veins, therefore, behave differently in this respect from the arteries (cf. page 201). The resistance of the veins to rupture by internal pressure, is, under normal conditions, very great, just as it is in the arteries.

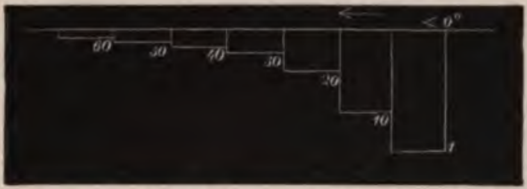

FIG. 92.—The cubic enlargement of the inferior vena cava of the cat, under uniformly increasing internal pressure, after Roy.

The essential physiological purpose of the veins is *to return the blood to the heart.* The force which drives the blood forward in the veins is the force of the heart itself. But the friction in the small arteries and in the capillaries, has by this time consumed the major part of the heart's driving power, consequently the total energy with which the blood flows in the veins is but a fractional part of the energy which it possessed as it left the heart. The greater part of that energy has been *transformed into heat* during the passage of the blood through the arteries and capillaries.

The *lateral pressure* in the veins is, therefore, much smaller than in the arteries. In the central veins of the thorax the blood pressure is negative because of the aspirating action of the thorax. In more peripheral veins it is positive and is higher the farther the vein from the heart, e. g., in the right jugular of the sheep, 0.2 mm. Hg., in the external facial 3.0, internal facial 5.2, brachial 4.1, in a branch of the latter 9.0, in the crural 11.4 mm. Hg. (Jacobson); in the superior vena cava of the dog close to its entrance into the right auricle — 3.0 mm. Hg., in the distal portion of the same vein −1.4, in the right external jugular −0.1, left external jugular 0.5, in the right brachial 3.9, in the left facial 5.1, left femoral 5.4, left saphena 7.4 mm. Hg. (Burton-Opitz). Observations on the sheep and on the dog, as will be seen, agree on the whole very closely.

After opening the thorax and thereby obliterating the negative intrathoracic pressure, the pressure in all the veins rises considerably, so that a negative pressure can no longer be demonstrated.

In order to determine the pressure in a vein it is necessary to avoid stoppage of the blood; a T-cannula is used and on account of the low pressure a soda solution is substituted for mercury in the manometer.

Just as in the arterial system, *the pressure in the veins* is conditioned upon the *quantity* of blood flowing from the heart in unit time, and upon the *resistance.* If the veins meet with great resistance in emptying their blood to the heart, the pressure in them increases. This happens for example when the heart is checked or brought to a standstill by stimulation of the vagus. In this case the heart is unable to drive forward all the blood which collects in the veins, and the consequent accumulation raises the venous pressure. If in spite of the inhibition, the right heart still expels in unit time just as much blood as it did before, the venous pressure suffers no change. The pressure in the veins is increased likewise if the lungs are highly inflated, for by this means the flow of blood into the intrathoracic veins is hindered, and it becomes more difficult for the right heart to empty itself.

On the other hand, the venous pressure falls as a result of all conditions favoring the return of the blood to the right heart or its discharge therefrom—e. g., acceleration after section of the vagus—provided the heart discharges in unit time a larger quantity of blood than before.

These influences take effect primarily on the central veins. In the periphery the pressure depends mainly upon the variations of blood volume and of resistance in the arteries. If an artery be completely clamped off, the pressure in the corresponding vein sinks to the level of the minimal pressure in the larger vein to which it is tributary. If a vein be clamped off, the pressure increases peripherally to the ligature because in this case the vein represents only a blind end of the artery.

The variations in pressure in the venæ cavæ give rise to pulsations in the larger veins of the trunk and the extremities, which are transmitted centrifugally with a velocity of one to three meters per second. The velocity of transmission through the jugular vein is greater than that through the vena cava to the crural vein (Morrow).

In order that the blood may flow uniformly, it is necessary that the *same quantity be delivered by the veins to the heart in unit time as is expelled by the heart into the arteries,* and this has been proved by the direct observations of Cyon and Steinmann, and of Burton-Opitz, to be the case. The volume of flow is, therefore, about the same in corresponding arteries and veins; but on account of the greater cross section of the veins, the linear velocity in them is less than in the arteries—e. g., in the external jugular of the dog 147 mm., in the femoral 62 mm. per second. After section of the vagi, the volume of the current in the jugular vein increases 2.8 times, but decreases about fifty-seven per cent on compression of both carotids (Burton-Opitz).

B. AIDS TO THE BLOOD FLOW IN THE VEINS

The blood flow in the veins can be very easily disturbed by all kinds of external influences; but to offset this we have several special mechanisms which favor the flow. One such is the *suction of the thorax* already discussed at page 176, as well as *that of the heart itself*. Besides these, several other conditions in connection with the *valves of the veins*, operate to prevent stasis of blood in the veins.

The valves of the veins discovered by Fabricius ab Aquapendente in 1574, are semilunar folds of the lining membrane, so arranged that they open toward the heart but prevent the flow of blood in the opposite direction. Two such valves as a rule stand opposite each other.

When external pressure of any kind is exerted upon a vein, the *backward flow of blood is checked* by the nearest valve, and it is compelled therefore to move in the direction of the heart. As a result we find that with every muscular contraction there is an increase in the quantity of blood flowing from the corresponding vein. If the muscle be thrown into tetanus, there follows at first an acceleration, then a retardation of the blood flow, which lasts until the tetanus abates, and the pressure on the vein caused by it ceases.

Thus Burton-Opitz found the volume of flow in the femoral vein in one experiment with a resting muscle to be 1.1 c.c. per second; with a tetanizing stimulus of the sciatic nerve, lasting 8.1 seconds, the volume was 4.0 c.c. during the contraction, 0.4 c.c. during complete tetanus, and after relaxation of the muscle 1.3 c.c.

Under ordinary circumstances clonic, cramplike contractions of the muscles never occur, but with every movement of the body contraction and relaxation alternate. Because of the intermittent pressure upon the veins which such an alternation produces, the usual muscular contractions must materially favor the movement of the blood in them.

Changing the attitudes of the body also is an important aid to the flow of venous blood.

The femoral vein under Poupart's ligament and in the fossa ovalis, becomes empty of blood and collapses when the thigh is turned outward and at the same time moved backward so as to stretch it as much as possible. It fills full again as soon as the leg is brought back to its former position or is brought still further forward or flexed as much as possible. These changes of position take place with every step which we make (Braune).

Finally, we have in the *stretching movements* of the body a means of accelerating the blood in the veins. When a vein is elongated without at the same time being compressed its cubic capacity is increased, and it then exerts a suction on the blood column. For the venous system of the upper extremities such a suction is obtained when with fists clinched and wrists bent, the arms are stretched horizontally and moved backward in a certain plane of rotation. A general state of relaxation and consequent stagnation are obtained when with fingers stretched and the hand flexed dorsally the arms are bent at the elbows and brought close to the thorax. The veins of the lower extremities are stretched when the thighs are spread apart and turned outward at the hip joint as far as possible, the knees and feet being at the same time extended. Flexion, adduction and turning of the thighs inward, bending of the knees and dorsal flexion of the feet bring about a

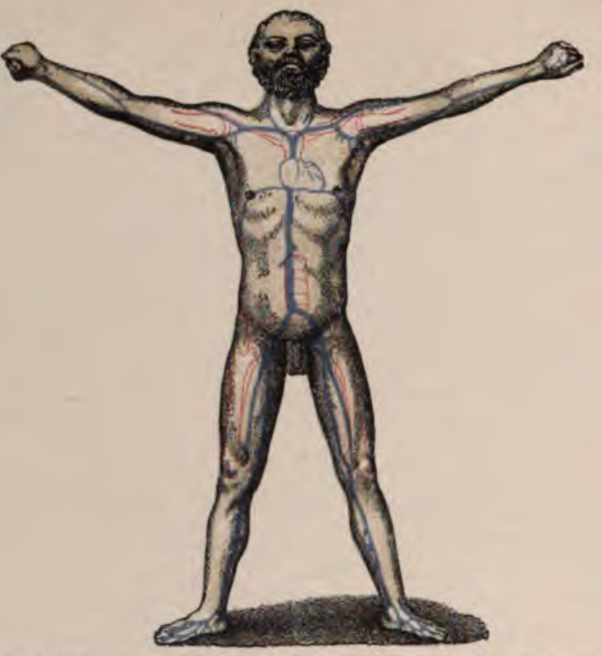

FIG. 93.—Position of the body in which the veins are stretched as much as possible, after Braune.

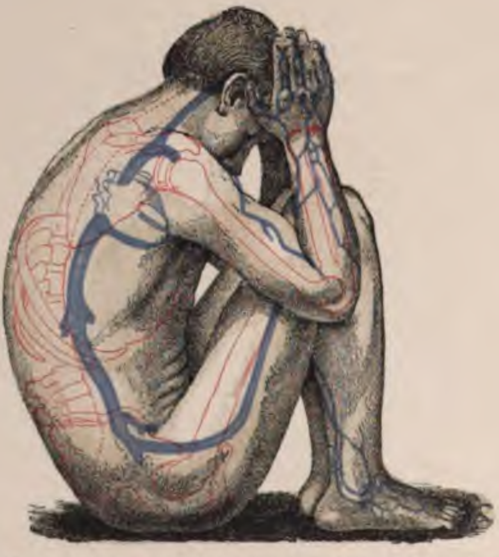

FIG. 94.—Position of the body in which the venous system is relaxed as much as possible, after Braune.

general relaxation of the same chief trunks. The position in which the venous system is in general stretched most strongly corresponds well with the attitude which one takes involuntarily when, after working at a desk for a long time, he stands up and stretches himself (Fig. 93). It is, therefore, to be assumed that such a stretching of the trunk and of the extremities acts favorably upon the venous circulation, which has been disturbed by sitting too long (Fig. 94), and this quite independently of the direct effect of muscles and fascia (Braune).

It may happen at times that a greater quantity of blood flows to the right heart than can be disposed of. This is possible, for example, when a powerful *vasoconstriction* occurs throughout a large vascular region. A large quantity of blood is then forced from the arteries into the veins, and from these to the right heart, while at the same time the discharge of blood from the left ventricle becomes more difficult on account of the high resistance in the contracted arteries.

We do not know how often or to what extent this may happen. We only know that after extirpation of the liver, the portal vein having been previously connected with the inferior vena cava, the heart is found dilated to its utmost, and the great veins are filled swelling full of blood (Stolnikow). The liver takes up a considerable quantity of blood like a sponge, and protects the right heart from an oversupply, just as it aids in the relief of the heart when overdistention occurs as a result of transfusion (cf. page 207).

§ 8. THE LESSER CIRCULATION AND THE RESPIRATORY VARIATIONS OF BLOOD PRESSURE

A. THE PULMONARY CIRCULATION

In general the same laws which we have learned in our study of the blood movements in the greater circulation hold good for the lesser circulation. The pressure is dependent upon the quantity of blood discharged from the right heart and upon the resistance in the pulmonary vessels. The quantity of blood which the right ventricle forces into the pulmonary arteries depends upon the quantity of blood which flows from the greater circulation through the venæ cavæ into the right heart. This quantity is determined partly by events in the aortic system, and partly by the pressure changes in the thoracic cavity which accompany the different phases of respiration.

Thus every hindrance of any moment to the flow of blood into the venæ cavæ reduces the pressure in the pulmonary arteries. An increased supply of blood to the right heart, such for example as is brought about by powerful contraction of the abdominal vessels, increases the pulmonary pressure.

We have already emphasized the fact that with each act of inspiration the thoracic cavity exerts suction on the blood vessels which enter it. The right ventricle, therefore, receives more blood during inspiration than during expiration; nevertheless the pressure in the ventricle itself (Talma) and in the pulmonary arteries (Knoll) declines only to rise again at the next expiration.

These variations of blood pressure are caused partly by the effect of variations in the intrathoracic pressure on the thin-walled right ventricle, and partly

by their effect on the diameter of the vessels in the lungs. The diameter of these vessels, as d'Arsonval, De Jager, Heger and others have shown, increases with the expansion of the lungs during inspiration, and decreases with the collapse of the lungs during expiration. Since the two factors operate in the same direction, there remains for us to determine to which of them the greater significance is to be ascribed. We must first inquire to what extent the resistance in the pulmonary vessels is changed by the different phases of respiration.

This question does not admit of a direct answer; but we have certain well-established facts which show very clearly that the *resistance in the pulmonary channels is in general so small* that only a considerable change in the diameter of the vessels could exercise upon it any very marked influence.

We should mention first the results which Lichtheim obtained by occluding a large part of the pulmonary vessels. It was shown with dogs which received artificial respiration by rhythmical inflation of the lungs, that about three-fourths of the territory supplied by the pulmonary arteries could be shut out without diminishing in the least the flow of blood to the left ventricle. Again, the left pleural cavity of a rabbit breathing naturally has been opened without interfering with the respiration on the other side, and the entire left lung tied off at the hilus: yet as a rule no fall of blood pressure was observed in the greater circulation.

We may say, then, that one-half (in curarized animals still less) of the pulmonary blood channel is enough to supply the necessary quantity of blood to the left heart. The explanation might be sought in an increased blood pressure in the lesser circulation and a consequent greater dilatation of the vessels which remain open. But the increase in pressure is so insignificant (it never amounts to more than a few millimeters of Hg.) that it is very doubtful whether it could produce such an effect. Again we might imagine a vasomotor influence upon the pulmonary vessels; but the facts which we have at present on this subject scarcely point to any considerable direct control of these vessels by the central nervous system. Finally, it is possible that under normal circumstances the lungs are never uniformly filled with blood, but that certain regions remain relatively empty, being made accessible to the blood only by unusual opportunities like that just mentioned.

Be this as it may, it certainly follows from the facts before us that the resistance in the pulmonary vessels is very small. This conclusion is confirmed also by facts which we possess concerning the velocity of the blood flow in the lungs. Stewart has shown, for example, that a foreign fluid injected into the jugular vein passes the lesser circulation in three to four seconds. When the lungs are inflated by a positive internal pressure sufficient to stop the flow of blood in the pulmonary vessels, and the lungs are then released, the pressure in the greater circulation returns to its normal height in three to four seconds.

In view of this low pressure in the pulmonary vessels, one hesitates to suppose that the changes in their diameter which take place in spontaneous respiration as the direct result of alterations in the lung tissue can play the more important part in determining the variations of blood pressure in the lesser circulation. The *changes in intrathoracic pressure* are much rather to be assigned the place of first importance. The pressure in the right ventricle falls in inspiration not chiefly because the vessels in the lungs dilate a little, but because the inspiratory suction distends the heart, and *vice versa.*

The blood pressure in the pulmonary arteries is very low on account of the low resistance in the smaller pulmonary vessels. On the average it amounts

in the dog to about 20 mm. Hg., in the cat to about 18 and in the rabbit to about 15 (cf. page 170).

As mentioned above (page 208), the pressure in the greater circulation in the same individual may exhibit great variations from one moment to another. The pulmonary circulation is entirely different in this respect, the pressure variations there being on the whole very small—scarcely ever more than 10–15 mm. under normal circumstances.

It follows that the work of the left ventricle must *vary in amount much more* than that of the right, and this is borne out also by the fact that the left ventricle becomes more or less fatigued, when the right is still entirely capable.

The lesser circulation is dependent upon the greater not only because it draws its supply from the venæ cavæ, but also because it must deliver its blood to the left ventricle and so is affected by the conditions of the blood flow from that chamber. If, for example, the left ventricle is unable, because of high resistance, to discharge all the blood coming to it, so that a certain quantity accumulates within this chamber, a state of affairs will finally be reached where the flow from the right heart is hindered, which in fact has been experimentally demonstrated (Waller).

In general, however, this reverse effect of the left heart on the right is *only slight*, a fact associated with the great capacity of the pulmonary vessels. The lungs serve the same purpose with respect to the flow of blood into the left heart as does the liver with respect to the flow of blood to the right (cf. page 227).

Moreover, the great capacity of the pulmonary vessels has this advantage, that in great respiratory distress where the vessels of the greater circulation are powerfully contracted, the greatest possible quantity of blood is exposed to the alveolar air and the greatest possible quantity of oxygen is therefore absorbed. By this means the blood is relieved of the products of combustion, and the influence which these exert through their stimulation of the vasomotor centers is diminished to some extent.

B. RESPIRATORY VARIATIONS OF BLOOD PRESSURE

Just as the lesser circulation is influenced in several respects *by* the greater, it in turn exerts no less an influence *upon* the greater. Consequently there appear in the aorta variations of blood pressure which are synchronous with the respiratory movements and are doubtless dependent upon these and upon the variations in the pulmonary circulation. The mechanism by which these influences are brought to bear are rather complicated, and we have to take into account the following conditions.

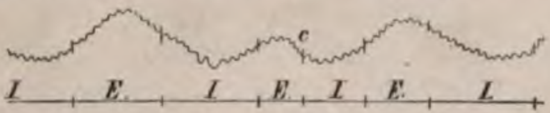

FIG. 95.—Variations of the aortic blood pressure in the dog, due to normal respiratory movements, after De Jager. *I*, inspiration; *E*, expiration. To be read from right to left.

The following circumstances tend during inspiration to *increase* the *blood pressure* in the aorta:

(1) The aspiration of the blood to the right heart increases;

(2) The diastole of the heart is favored;

(3) The flow of the blood in the pulmonary vessels is facilitated because of their dilatation;

(4) The pressure in the abdominal cavity increases because of the descent of the diaphragm; and the blood is forced in greater quantity to the right heart.

The following circumstances tend to *lower* the *aortic pressure:*

(1) The heart systole is rendered more difficult because of the increased suction in the thorax;

(2) At the beginning of inspiration, while the pulmonary vessels are still dilating, a part of the blood expelled from the right ventricle must remain in them, and by this means the mass of blood flowing from the left heart decreases until the pulmonary vessels have been filled, after which the flow is increased.

In expiration naturally these mechanisms work in the reverse direction.

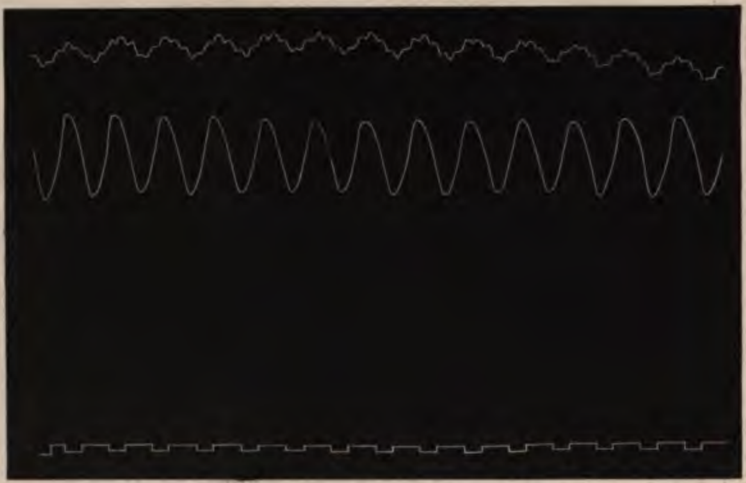

FIG. 96.—Respiratory variations of blood pressure in the rabbit. To be read from right to left. The upper line represents the blood pressure, the middle line the respiratory movements (downward stroke, inspiration), the lower line the time record in seconds.

Among these factors the *alterations of blood flow* to the right heart is of the first importance. The respiratory variations of the aortic pressure witnessed in a dog breathing quietly (Fig. 95) could be explained therefore in the following manner. In expiration the right heart has less blood at its disposal, the left heart receives less blood, and the aortic pressure falls. When inspiration sets in, and the flow to the right heart becomes greater, it can drive a greater quantity to the left heart, and the aortic pressure rises. But a short time must always elapse before this increased supply to the right heart can be felt in the left heart and in the aorta; hence at the beginning of inspiration the pressure is still falling. Likewise at the very beginning of the following expiration the right heart still has at its disposal a portion of the increased supply; the rise in pressure in the aorta continues therefore for a moment until the diminished supply to the right heart can be felt on the left, when the aortic pressure begins to fall.

When the rate of respiration is somewhat more frequent (cf. Fig. 96), the influence of expiration is felt for the first during the following inspiration and *vice versa*; the aortic pressure rises therefore during expiration and falls during inspiration.

In still more frequent and shallow breathing the variations of the flow to the right heart are so slight that no respiratory variations of blood pressure appear in the greater circulation.

Besides these, certain nervous events exercise an unmistakable influence on the respiratory variations of blood pressure in the aorta. During expiration the pulse rate decreases in consequence of an automatic stimulation of the vagus (depressor effect), and the vascular tonus increases as the result of an automatic stimulation of the vasomotor nerves (pressor effect). These factors make themselves felt only with a rhythm which is not too rapid, and even then they may not be able to alter the course of variations in the aortic pressure produced by the mechanical factors already discussed.

Still other more or less regular variations of pressure (Traube-Hering waves) occur in the aortic system, which may run parallel with certain periodic variations in the frequency and depth of respiration extending over several respiratory cycles (Cheyne-Stokes breathing, Chapter IX) or may be entirely independent of them. But further discussion of their nature would lead us too far at this time.

Artificial respiration gives in all respects just the reverse effects of natural respiration. Thus with inflation of the lungs the blood flow to the right heart is rendered more difficult on account of the positive intrapulmonary pressure, and the resulting compression of pulmonary vessels. The consequence is that the aortic pressure rises at the beginning of inflation, and falls again in the further course of the same phase.

The cause of these artificial pressure variations must be mainly the *alterations in diameter of the pulmonary vessels.* At the beginning of inflation the blood pressure rises because of the compression produced and the consequent emptying of the blood toward the heart. The subsequent fall is the result of the increased resistance in the pulmonary vessels. At the beginning of the artificial collapse a certain quantity of blood remains behind in the dilated vessels and the pressure sinks still farther until the influence of diminished resistance in the pulmonary vessels makes itself felt and the left heart is more abundantly supplied.

§ 9. VASOCONSTRICTOR NERVES

The muscular coat of the blood vessels is under the influence of two kinds of nerve fibers, namely, those through whose excitation the muscle fibers are caused to contract (*vasoconstrictor nerves*), and those through whose excitation the muscle fibers are caused to relax (*vasodilator nerves*). The former were discovered by Claude Bernard and Brown-Séquard (1851, 1852), the latter by Schiff (1855) and Claude Bernard (1858). The importance of the vasomotor nerves for the circulation was first clearly established by Ludwig (1864).

If the *cervical sympathetic be cut*, one observes among other things that the vessels of the ear dilate so that small arteries and veins which were formerly invisible now stand out clearly. If the edge of the ear be snipped off, blood flows more freely from the wound than before section of the nerve. The temperature of the ear is higher than that of the other side. Blood flows

(2) The diastole of the heart is favored;

(3) The flow of the blood in the pulmonary vessels is facilitated because of their dilatation;

(4) The pressure in the abdominal cavity increases because of the descent of the diaphragm; and the blood is forced in greater quantity to the right heart.

The following circumstances tend to *lower* the *aortic pressure:*

(1) The heart systole is rendered more difficult because of the increased suction in the thorax;

(2) At the beginning of inspiration, while the pulmonary vessels are still dilating, a part of the blood expelled from the right ventricle must remain in them, and by this means the mass of blood flowing from the left heart decreases until the pulmonary vessels have been filled, after which the flow is increased.

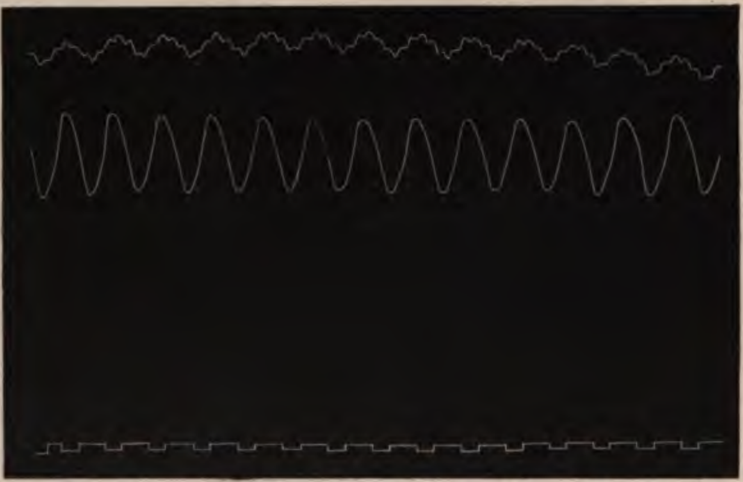

FIG. 96.—Respiratory variations of blood pressure in the rabbit. To be read from right to left. The upper line represents the blood pressure, the middle line the respiratory movements (downward stroke, inspiration), the lower line the time record in seconds.

In expiration naturally these mechanisms work in the reverse direction.

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If now the *end* of the *cervical sympathetic toward the head be stimulated,* the arteries are constricted—with powerful stimulation, so much so that their lumen disappears; the venous blood flows slowly and has a dark color; the blood flows but feebly from a fresh cut, and the temperature of the ear falls.

Since section of the cervical sympathetic causes a vasodilation of the ear, and its stimulation constricts the blood vessels in the same ear, it follows that this nerve must contain fibers which preside over contraction of the muscular coat in these vessels—i. e., which are vasoconstrictor fibers for the ear. It follows moreover that these nerves must be under *tonic*—i. e., *continuous—stimulation* from the central nervous system.

Now we have nerves running to all, or at least to most, of the arterial regions of the body, which have the same properties as those just described. The vascular tonus maintained by their constant stimulation is of the utmost importance. For should all the vessels for any reason be completely relaxed, there would collect in them, especially in the veins, so great a quantity of blood that the volume flowing back to the heart would not be sufficient to maintain the necessary supply; the blood pressure would fall to a low level and, although the heart might continue to act for a time, it would be unable to accomplish anything. All of which means that the total quantity of blood in the body is sufficient to fill the blood vessels to the proper extent, only when they are partially constricted.

The vasoconstrictors are given off from the central nervous system in the anterior nerve roots, and are distributed to the sympathetic paths throughout the whole body. The following results have been obtained so far with regard to their course:

Most of the vasoconstrictor nerves pass out from the thoracic portion of the spinal cord. The nerves running to the head arise from the first to the fifth thoracic nerves, pass over into the cervical sympathetic and are distributed to the *different parts of the head.* This is attested by the fact that stimulation of the cervical sympathetic causes vasoconstriction in all the organs of the head. With regard to the brain, however, results are less positive. While some authors assert that they have found vasoconstrictor nerves for the brain in the cervical sympathetic, others have come to the conclusion that although nerve fibers have been demonstrated anatomically for the blood vessels of the brain, in general the blood supply to this organ is not regulated by means of vasomotor nerves, but by alterations in the supply to other organs of the body.

With respect to the further course of these nerves to the head, our information is very incomplete. According to some they pass over into the sympathetic plexuses surrounding the blood vessels, according to others they unite with the cranial nerves. The latter has been demonstrated for the *tongue* at least, since its vasoconstrictor nerves run for the most part in the hypoglossal.

The vasoconstrictor nerves of the *anterior extremities* pass out from the spinal cord in the third to the tenth thoracic nerves, those of the posterior extremities in the eleventh thoracic to the third lumbar nerves. It is stated also that the vasoconstrictor nerves of the toes are contained in the sixth lumbar to the first sacral nerves.

The *tail* gets its vasoconstrictor nerves from the third to the fourth lumbar nerves; and the *dorsal side of the trunk* from the posterior branches of the spinal nerves corresponding to the different segments of the back.

The nerves pass from their origin through the trunk of the sympathetic and from there for the most part to the different organs of the body by way of the chief nerve trunks.

The vasoconstrictor nerves of the *abdominal viscera* leave the spinal cord by the third thoracic to the first or third lumbar nerves, run for the most part in the splanchnics, and are distributed by them to the different organs of the abdominal cavity. The nerves of the *large intestine* pass out of the spinal cord in the seventh thoracic to the second lumbar nerves; those of the *liver* in the sixth thoracic to the second lumbar; those of the *pancreas* in the fifth thoracic to the first lumbar nerve.

The vasoconstrictor nerves of the *organs of generation* pass out in the last lumbar and in the first sacral nerves, and proceed to their end arborizations through the hypogastric plexus.

The *lungs* also possess vasoconstrictor nerves; according to the majority of authors, they leave the spinal cord in the second to the fifth thoracic nerves, and proceed by way of the sympathetic paths to the lungs. Recently the presence of vasomotor nerves in the lungs has been absolutely denied.

Vasoconstrictor nerves appear to traverse other paths also. Thus we find in the second and third nerves of the cervical plexus vasoconstrictor fibers for the tip and lateral parts of the ear, which reach their destination by way of the auricularis cervicalis nerve. It is further asserted that the vagus conveys vasoconstrictor nerves to the *heart*, to the *stomach*, to the *intestine* (not confirmed by all authors) and to the *kidneys*, and also that in it are contained vasoconstrictor fibers for the *lungs*. It is indeed not impossible that these fibers might arise from the sympathetic (since it is definitely asserted that the vasoconstrictor nerves in the auricularis cervicalis arise in the thoracic sympathetic and run through the stellate ganglion), and it is also conceivable that they actually belong to the branches of the vagus.

Because of the great vascular territory committed to their control the *splanchnics* play the most important part of all vasomotor nerves. For this reason the blood pressure falls after bilateral section of these nerves, and shows a very great rise on stimulation of them.

Constricting nerve fibers have been demonstrated also for the *veins*. If the aorta be tied off immediately below the origin of the left subclavian, and the blood supply to the hinder part of the body be thereby cut off, stimulation of the splanchnics drives through the inferior vena cava into the right heart a quantity of blood which runs up to twenty-seven per cent of the total quantity in the animal. According to Mall, this is caused by contraction of the portal system.

Constrictor effects of nerve stimulation in other veins are mentioned by different authors; but R. F. Fuchs has published experiments in which he obtained no active constriction of the veins either by direct stimulation of the veins themselves or by electrical stimulation of nerves, wherefore he denies entirely the presence of vasomotor nerves for the veins.

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This question does not admit of a direct answer; but we have certain well-established facts which show very clearly that the *resistance in the pulmonary channels is in general so small* that only a considerable change in the diameter of the vessels could exercise upon it any very marked influence.

We should mention first the results which Lichtheim obtained by occluding a large part of the pulmonary vessels. It was shown with dogs which received artificial respiration by rhythmical inflation of the lungs, that about three-fourths of the territory supplied by the pulmonary arteries could be shut out without diminishing in the least the flow of blood to the left ventricle. Again, the left pleural cavity of a rabbit breathing naturally has been opened without interfering with the respiration on the other side, and the entire left lung tied off at the hilus: yet as a rule no fall of blood pressure was observed in the greater circulation.

We may say, then, that one-half (in curarized animals still less) of the pulmonary blood channel is enough to supply the necessary quantity of blood to the left heart. The explanation might be sought in an increased blood pressure in the lesser circulation and a consequent greater dilatation of the vessels which remain open. But the increase in pressure is so insignificant (it never amounts to more than a few millimeters of Hg.) that it is very doubtful whether it could produce such an effect. Again we might imagine a vasomotor influence upon the pulmonary vessels; but the facts which we have at present on this subject scarcely point to any considerable direct control of these vessels by the central nervous system. Finally, it is possible that under normal circumstances the lungs are never uniformly filled with blood, but that certain regions remain relatively empty, being made accessible to the blood only by unusual opportunities like that just mentioned.

Be this as it may, it certainly follows from the facts before us that the resistance in the pulmonary vessels is very small. This conclusion is confirmed also by facts which we possess concerning the velocity of the blood flow in the lungs. Stewart has shown, for example, that a foreign fluid injected into the jugular vein passes the lesser circulation in three to four seconds. When the lungs are inflated by a positive internal pressure sufficient to stop the flow of blood in the pulmonary vessels, and the lungs are then released, the pressure in the greater circulation returns to its normal height in three to four seconds.

In view of this low pressure in the pulmonary vessels, one hesitates to suppose that the changes in their diameter which take place in spontaneous respiration as the direct result of alterations in the lung tissue can play the more important part in determining the variations of blood pressure in the lesser circulation. The *changes in intrathoracic pressure* are much rather to be assigned the place of first importance. The pressure in the right ventricle falls in inspiration not chiefly because the vessels in the lungs dilate a little, but because the inspiratory suction distends the heart, and *vice versa.*

The blood pressure in the pulmonary arteries is very low on account of the low resistance in the smaller pulmonary vessels. On the average it amounts

in the dog to about 20 mm. Hg., in the cat to about 18 and in the rabbit to about 15 (cf. page 170).

As mentioned above (page 208), the pressure in the greater circulation in the same individual may exhibit great variations from one moment to another. The pulmonary circulation is entirely different in this respect, the pressure variations there being on the whole very small—scarcely ever more than 10–15 mm. under normal circumstances.

It follows that the work of the left ventricle must *vary in amount much more* than that of the right, and this is borne out also by the fact that the left ventricle becomes more or less fatigued, when the right is still entirely capable.

The lesser circulation is dependent upon the greater not only because it draws its supply from the venæ cavæ, but also because it must deliver its blood to the left ventricle and so is affected by the conditions of the blood flow from that chamber. If, for example, the left ventricle is unable, because of high resistance, to discharge all the blood coming to it, so that a certain quantity accumulates within this chamber, a state of affairs will finally be reached where the flow from the right heart is hindered, which in fact has been experimentally demonstrated (Waller).

In general, however, this reverse effect of the left heart on the right is *only slight*, a fact associated with the great capacity of the pulmonary vessels. The lungs serve the same purpose with respect to the flow of blood into the left heart as does the liver with respect to the flow of blood to the right (cf. page 227).

Moreover, the great capacity of the pulmonary vessels has this advantage, that in great respiratory distress where the vessels of the greater circulation are powerfully contracted, the greatest possible quantity of blood is exposed to the alveolar air and the greatest possible quantity of oxygen is therefore absorbed. By this means the blood is relieved of the products of combustion, and the influence which these exert through their stimulation of the vasomotor centers is diminished to some extent.

B. RESPIRATORY VARIATIONS OF BLOOD PRESSURE

Just as the lesser circulation is influenced in several respects *by* the greater, it in turn exerts no less an influence *upon* the greater. Consequently there

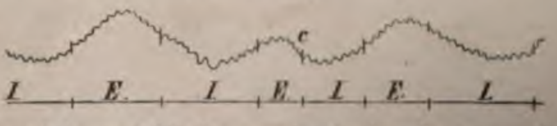

FIG. 95.—Variations of the aortic blood pressure in the dog, due to normal respiratory [illegible] ments, after De Jager. *I*, inspiration; *E*, expiration. To be read from right [illegible]

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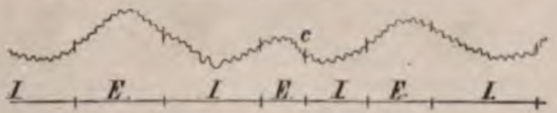

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The following circumstances tend during inspiration to *increase* the *blood pressure* in the aorta:

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Be this as it may, it certainly follows from the facts before us that the resistance in the pulmonary vessels is very small. This conclusion is confirmed also by facts which we possess concerning the velocity of the blood flow in the lungs. Stewart has shown, for example, that a foreign fluid injected into the jugular vein passes the lesser circulation in three to four seconds. When the lungs are inflated by a positive internal pressure sufficient to stop the flow of blood in the pulmonary vessels, and the lungs are then released, the pressure in the greater circulation returns to its normal height in three to four seconds.

In view of this low pressure in the pulmonary vessels, one hesitates to suppose that the changes in their diameter which take place in spontaneous respiration as the direct result of alterations in the lung tissue can play the more important part in determining the variations of blood pressure in the lesser circulation. The *changes in intrathoracic pressure* are much rather to be assigned the place of first importance. The pressure in the right ventricle falls in inspiration not chiefly because the vessels in the lungs dilate a little, but because the inspiratory suction distends the heart, and *vice versa*.

The blood pressure in the pulmonary arteries is very low on account of the low resistance in the smaller pulmonary vessels. On the average it amounts

in the dog to about 20 mm. Hg., in the cat to about 18 and in the rabbit to about 15 (cf. page 170).

As mentioned above (page 208), the pressure in the greater circulation in the same individual may exhibit great variations from one moment to another. The pulmonary circulation is entirely different in this respect, the pressure variations there being on the whole very small—scarcely ever more than 10–15 mm. under normal circumstances.

It follows that the work of the left ventricle must *vary in amount much more* than that of the right, and this is borne out also by the fact that the left ventricle becomes more or less fatigued, when the right is still entirely capable.

The lesser circulation is dependent upon the greater not only because it draws its supply from the venæ cavæ, but also because it must deliver its blood to the left ventricle and so is affected by the conditions of the blood flow from that chamber. If, for example, the left ventricle is unable, because of high resistance, to discharge all the blood coming to it, so that a certain quantity accumulates within this chamber, a state of affairs will finally be reached where the flow from the right heart is hindered, which in fact has been experimentally demonstrated (Waller).

In general, however, this reverse effect of the left heart on the right is *only slight*, a fact associated with the great capacity of the pulmonary vessels. The lungs serve the same purpose with respect to the flow of blood into the left heart as does the liver with respect to the flow of blood to the right (cf. page 227).

Moreover, the great capacity of the pulmonary vessels has this advantage, that in great respiratory distress where the vessels of the greater circulation are powerfully contracted, the greatest possible quantity of blood is exposed to the alveolar air and the greatest possible quantity of oxygen is therefore absorbed. By this means the blood is relieved of the products of combustion, and the influence which these exert through their stimulation of the vasomotor centers is diminished to some extent.

B. RESPIRATORY VARIATIONS OF BLOOD PRESSURE

Just as the lesser circulation is influenced in several respects *by* the greater, it in turn exerts no less an influence *upon* the greater. Consequently there appear in the aorta variations of blood pressure which are synchronous with the respiratory movements and are doubtless dependent upon these and upon the variations in the pulmonary circulation. The mechanism by which these influences are brought to bear are rather complicated, and we have to take into account the following conditions.

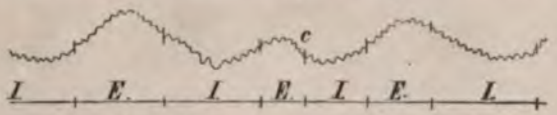

FIG. 95.—Variations of the aortic blood pressure in the dog, due to normal respiratory movements, after De Jager. *I*, inspiration; *E*, expiration. To be read from right to left.

The following circumstances tend during inspiration to *increase* the *blood pressure* in the aorta:

(1) The aspiration of the blood to the right heart increases;

(2) The diastole of the heart is favored;

(3) The flow of the blood in the pulmonary vessels is facilitated because of their dilatation;

(4) The pressure in the abdominal cavity increases because of the descent of the diaphragm; and the blood is forced in greater quantity to the right heart.

The following circumstances tend to *lower* the *aortic pressure:*

(1) The heart systole is rendered more difficult because of the increased suction in the thorax;

(2) At the beginning of inspiration, while the pulmonary vessels are still dilating, a part of the blood expelled from the right ventricle must remain in them, and by this means the mass of blood flowing from the left heart decreases until the pulmonary vessels have been filled, after which the flow is increased.

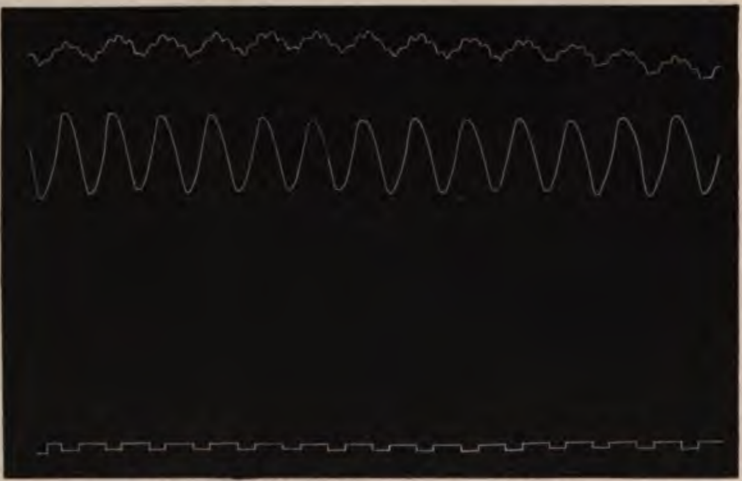

FIG. 96.—Respiratory variations of blood pressure in the rabbit. To be read from right to left. The upper line represents the blood pressure, the middle line the respiratory movements (downward stroke, inspiration), the lower line the time record in seconds.

In expiration naturally these mechanisms work in the reverse direction.

Among these factors the *alterations of blood flow* to the right heart is of the first importance. The respiratory variations of the aortic pressure witnessed in a dog breathing quietly (Fig. 95) could be explained therefore in the following manner. In expiration the right heart has less blood at its disposal, the left heart receives less blood, and the aortic pressure falls. When inspiration sets in, and the flow to the right heart becomes greater, it can drive a greater quantity to the left heart, and the aortic pressure rises. But a short time must always elapse before this increased supply to the right heart can be felt in the left heart and in the aorta; hence at the beginning of inspiration the pressure is still falling. Likewise at the very beginning of the following expiration the right heart still has at its disposal a portion of the increased supply; the rise in pressure in the aorta continues therefore for a moment until the diminished supply to the right heart can be felt on the left, when the aortic pressure begins to fall.

When the rate of respiration is somewhat more frequent (cf. Fig. 96), the influence of expiration is felt for the first during the following inspiration and *vice versa*; the aortic pressure rises therefore during expiration and falls during inspiration.

In still more frequent and shallow breathing the variations of the flow to the right heart are so slight that no respiratory variations of blood pressure appear in the greater circulation.

Besides these, certain nervous events exercise an unmistakable influence on the respiratory variations of blood pressure in the aorta. During expiration the pulse rate decreases in consequence of an automatic stimulation of the vagus (depressor effect), and the vascular tonus increases as the result of an automatic stimulation of the vasomotor nerves (pressor effect). These factors make themselves felt only with a rhythm which is not too rapid, and even then they may not be able to alter the course of variations in the aortic pressure produced by the mechanical factors already discussed.

Still other more or less regular variations of pressure (Traube-Hering waves) occur in the aortic system, which may run parallel with certain periodic variations in the frequency and depth of respiration extending over several respiratory cycles (Cheyne-Stokes breathing, Chapter IX) or may be entirely independent of them. But further discussion of their nature would lead us too far at this time.

Artificial respiration gives in all respects just the reverse effects of natural respiration. Thus with inflation of the lungs the blood flow to the right heart is rendered more difficult on account of the positive intrapulmonary pressure, and the resulting compression of pulmonary vessels. The consequence is that the aortic pressure rises at the beginning of inflation, and falls again in the further course of the same phase.

The cause of these artificial pressure variations must be mainly the *alterations in diameter of the pulmonary vessels.* At the beginning of inflation the blood pressure rises because of the compression produced and the consequent emptying of the blood toward the heart. The subsequent fall is the result of the increased resistance in the pulmonary vessels. At the beginning of the artificial collapse a certain quantity of blood remains behind in the dilated vessels and the pressure sinks still farther until the influence of diminished resistance in the pulmonary vessels makes itself felt and the left heart is more abundantly supplied.

§ 9. VASOCONSTRICTOR NERVES

The muscular coat of the blood vessels is under the influence of two kinds of nerve fibers, namely, those through whose excitation the muscle fibers are caused to contract (*vasoconstrictor nerves*), and those through whose excitation the muscle fibers are caused to relax (*vasodilator nerves*). The former were discovered by Claude Bernard and Brown-Séquard (1851, 1852), the latter by Schiff (1855) and Claude Bernard (1858). The importance of the vasomotor nerves for the circulation was first clearly established by Ludwig (1864).

If the *cervical sympathetic be cut,* one observes among other things that the vessels of the ear dilate so that small arteries and veins which were formerly invisible now stand out clearly. If the edge of the ear be snipped off, blood flows more freely from the wound than before section of the nerve. The temperature of the ear is higher than that of the other side. Blood flows more rapidly through the organ and does not have time to undergo the changes which it otherwise would in the capillaries; the color of the venous blood is therefore lighter, and its properties are similar to those of arterial blood.

If now the *end* of the *cervical sympathetic toward the head be stimulated,* the arteries are constricted—with powerful stimulation, so much so that their lumen disappears; the venous blood flows slowly and has a dark color; the blood flows but feebly from a fresh cut, and the temperature of the ear falls.

Since section of the cervical sympathetic causes a vasodilation of the ear, and its stimulation constricts the blood vessels in the same ear, it follows that this nerve must contain fibers which preside over contraction of the muscular coat in these vessels—i. e., which are vasoconstrictor fibers for the ear. It follows moreover that these nerves must be under *tonic*—i. e., *continuous—stimulation* from the central nervous system.

Now we have nerves running to all, or at least to most, of the arterial regions of the body, which have the same properties as those just described. The vascular tonus maintained by their constant stimulation is of the utmost importance. For should all the vessels for any reason be completely relaxed, there would collect in them, especially in the veins, so great a quantity of blood that the volume flowing back to the heart would not be sufficient to maintain the necessary supply; the blood pressure would fall to a low level and, although the heart might continue to act for a time, it would be unable to accomplish anything. All of which means that the total quantity of blood in the body is sufficient to fill the blood vessels to the proper extent, only when they are partially constricted.

The vasoconstrictors are given off from the central nervous system in the anterior nerve roots, and are distributed to the sympathetic paths throughout the whole body. The following results have been obtained so far with regard to their course:

Most of the vasoconstrictor nerves pass out from the thoracic portion of the spinal cord. The nerves running to the head arise from the first to the fifth thoracic nerves, pass over into the cervical sympathetic and are distributed to the *different parts of the head.* This is attested by the fact that stimulation of the cervical sympathetic causes vasoconstriction in all the organs of the head. With regard to the brain, however, results are less positive. While some authors assert that they have found vasoconstrictor nerves for the brain in the cervical sympathetic, others have come to the conclusion that although nerve fibers have been demonstrated anatomically for the blood vessels of the brain, in general the blood supply to this organ is not regulated by means of vasomotor nerves, but by alterations in the supply to other organs of the body.

With respect to the further course of these nerves to the head, our information is very incomplete. According to some they pass over into the sympathetic plexuses surrounding the blood vessels, according to others they unite with the cranial nerves. The latter has been demonstrated for the *tongue* at least, since its vasoconstrictor nerves run for the most part in the hypoglossal.

The vasoconstrictor nerves of the *anterior extremities* pass out from the spinal cord in the third to the tenth thoracic nerves, those of the posterior extremities in the eleventh thoracic to the third lumbar nerves. It is stated also that the vasoconstrictor nerves of the toes are contained in the sixth lumbar to the first sacral nerves.

The *tail* gets its vasoconstrictor nerves from the third to the fourth lumbar nerves; and the *dorsal side of the trunk* from the posterior branches of the spinal nerves corresponding to the different segments of the back.

The nerves pass from their origin through the trunk of the sympathetic and from there for the most part to the different organs of the body by way of the chief nerve trunks.

The vasoconstrictor nerves of the *abdominal viscera* leave the spinal cord by the third thoracic to the first or third lumbar nerves, run for the most part in the splanchnics, and are distributed by them to the different organs of the abdominal cavity. The nerves of the *large intestine* pass out of the spinal cord in the seventh thoracic to the second lumbar nerves; those of the *liver* in the sixth thoracic to the second lumbar; those of the *pancreas* in the fifth thoracic to the first lumbar nerve.

The vasoconstrictor nerves of the *organs of generation* pass out in the last lumbar and in the first sacral nerves, and proceed to their end arborizations through the hypogastric plexus.

The *lungs* also possess vasoconstrictor nerves; according to the majority of authors, they leave the spinal cord in the second to the fifth thoracic nerves, and proceed by way of the sympathetic paths to the lungs. Recently the presence of vasomotor nerves in the lungs has been absolutely denied.

Vasoconstrictor nerves appear to traverse other paths also. Thus we find in the second and third nerves of the cervical plexus vasoconstrictor fibers for the tip and lateral parts of the ear, which reach their destination by way of the auricularis cervicalis nerve. It is further asserted that the vagus conveys vasoconstrictor nerves to the *heart*, to the *stomach*, to the *intestine* (not confirmed by all authors) and to the *kidneys*, and also that in it are contained vasoconstrictor fibers for the *lungs*. It is indeed not impossible that these fibers might arise from the sympathetic (since it is definitely asserted that the vasoconstrictor nerves in the auricularis cervicalis arise in the thoracic sympathetic and run through the stellate ganglion), and it is also conceivable that they actually belong to the branches of the vagus.

Because of the great vascular territory committed to their control the *splanchnics* play the most important part of all vasomotor nerves. For this reason the blood pressure falls after bilateral section of these nerves, and shows a very great rise on stimulation of them.

Constricting nerve fibers have been demonstrated also for the *veins*. If the aorta be tied off immediately below the origin of the left subclavian, and the blood supply to the hinder part of the body be thereby cut off, stimulation of the splanchnics drives through the inferior vena cava into the right heart a quantity of blood which runs up to twenty-seven per cent of the total quantity in the animal. According to Mall, this is caused by contraction of the portal system.

Constrictor effects of nerve stimulation in other veins are mentioned by different authors; but R. F. Fuchs has published experiments in which he obtained no active constriction of the veins either by direct stimulation of the veins themselves or by electrical stimulation of nerves, wherefore he denies entirely the presence of vasomotor nerves for the veins.

Finally, the musculature of the vessels contracts under high internal pres-

sure and relaxes in consequence of a fall in pressure. According to Bayliss these changes are entirely independent of the central nervous system and can be demonstrated under natural conditions as well as in exsected arteries.

§ 10. VASODILATOR NERVES

If the lingual nerve be stimulated, and attention be directed to the submaxillary gland, the vessels of the gland may be seen to dilate. The veins of the gland swell up, the blood flowing in them takes on a brighter color, and sometimes actual pulsations appear in them. From this it follows that this nerve contains fibers, the stimulation of which cause the vessels of the gland to dilate. Such nerves are described as *vasodilator nerves.*

Where these nerves occur unmixed with vasoconstrictor nerves, one meets with no difficulty in demonstrating them. Where they are mixed with such nerves for the same organ, it is necessary to adopt a special order of experimentation, because the vasoconstrictor effect of stimulation often, if not always, predominates. A strong vasodilation appears as an after-effect of the simultaneous stimulation of both kinds of nerves. The two are, therefore, not strictly antagonistic, but must affect the vessels at different points, just as the two kinds of cardiac nerves have different points of application in the heart (V. Frey; cf. page 193).

On the other hand, weak stimulation of the constrictor nerves is overcome by stronger stimulation of the dilators. This appears, for example, in the case of the submaxillary gland with the cervical sympathetic intact. Although the vessels of the submaxillary gland are under the influence of the constrictor fibers contained in this nerve, stimulation of the lingual produces vasodilation.

If a nerve trunk be cut in two transversely, and the animal be allowed to live, *degeneration* of the peripheral stump appears in a short time. If the degenerating nerve be stimulated some *four days after the section,* vasodilation is obtained (Goltz), whereas stimulation of the fresh nerve causes vasoconstriction. This means that the dilator nerves retain their irritability somewhat longer than the constrictor nerves after connection with the central nervous system has been destroyed.

By appropriate variation of the stimulus the presence of dilator fibers can be demonstrated also in freshly cut nerves. Thus it has been shown that the latter are more irritable than the constrictor nerves if the *stimulus is weak* or is *applied rhythmically at a slow rate* (Ostroumoff, Bowditch).

Finally, it has been found that even if the two kinds of nerve fibers run in the same peripheral nerve trunk, they make their exit by way of *different roots of the spinal cord,* and can be separated one from the other by this means (Dastre and Morat).

Other characteristics of the dilator nerves are the following: (1) the latent period for their stimulation appears to be somewhat longer than that of the constrictor nerves; (2) whereas the maximum effect of the constrictors is quickly reached, that of the dilators takes more time; (3) the *after-effect* is longer.

The Course of the Vasodilator Nerves.—We have already become acquainted with the vasodilator nerves which traverse the lingual nerve to the *submaxillary* *gland.* They come from the facial and pass by way of the chorda tympani to the lingual. In the same path are found also the dilator nerves for the anterior two-thirds or three-fourths of the *tongue.* The dilator fibers for the posterior part of the tongue, for the anterior pillars of the *fauces,* and the *tonsils* run in the trunk of the *glossopharyngeal.*

The vasodilator fibers of the mucous membrane of the *lips,* the *cheeks,* the *hard palate* and the *external nares,* as well as of the corresponding parts of the *skin of the face* comes from the second to the fifth thoracic nerves, traverse the cervical sympathetic and unite for the most part with the trigeminal, which itself also contains fibers of this kind for the face and for the eye (Dastre and Morat).

The *ear* gets its dilator fibers from the eighth cervical and first thoracic nerves.

The dilator nerves of the *anterior extremities* leave the spinal cord from the fifth to the eighth thoracic: those of the posterior extremities probably in the second to the fourth lumbar nerves. Here we meet with the remarkable circumstance that the latter nerves pass out exclusively in the *posterior roots* of the lumbar nerves (Stricker, Bayliss; cf. Chapter XXII). The presence of vasodilator nerves in the posterior roots of the brachial plexus has been asserted also. We have the following facts with regard to the dilator nerves of the *abdominal organs:* Vasodilator fibers in abundance are found in the second to twelfth thoracic as well as in the first and second lumbar nerves of the dog: the twelfth and thirteenth thoracic contain a number of these in their *dorsal roots*; the splanchnics and the upper thoracic nerves contain the vasodilator fibers for the organs of the abdomen.

The vagus is said to convey vasodilator nerves for the *coronary arteries of the heart.* Most of the dilator nerves for the coronary vessels however traverse the sympathetic pathways. They probably pass out of the spinal cord, and reach the heart by way of the stellate ganglion (cf. Fig. 67, page 191).

According to some authors the *lungs* receive dilator fibers from the cervical sympathetic as well as from the vagus.

The vessels of the mucous membrane of the *larynx* are provided with dilator nerves from the superior laryngeal.

Vasodilator nerves which play an essential rôle in the erection of the *penis* pass to that organ by way of the anterior roots of the first to the third sacral nerves, and the hypogastric plexus.

§ 11. VASOMOTOR REFLEXES

Like the cardiac nerves, the *vasomotor nerves are stimulated reflexly,* and the blood supply to the various organs as well as the arterial blood pressure is variously influenced.

We have different observations tending to show that vasomotor reflexes can be discharged by the *vessels themselves,* so that the vessels may be said to participate in the reflex regulation of their own functions. We know also that these reflexes are set up by all other possible kinds of afferent nerves.

The reflex takes effect *primarily in the same vascular region whence came the afferent impulse.* Possibly the congestion which has long been known to take place on rubbing or warming the skin belongs to this class of reflexes, also the congestion which is seen in the intestine when the abdominal cavity is opened.

Generally speaking the result of these localized reflexes is a vasodilation, but under certain circumstances vasoconstriction may be the result. The reflex may spread to the corresponding part of the body on the *opposite side,* and not infrequently parts *far removed* from the region innervated by the afferent nerve show a reflex constriction or dilation of their vessels. Thus the vast *region innervated by the splanchnics* is very easily constricted by stimulation of all possible kinds of sensory nerves. It may also be dilated as the result of a sensory excitation. The *vessels of the skeletal muscles* as a rule appear to be dilated by sensory impulses. The dilation appears first in the muscles which stand in close functional relationship with the nerves stimulated; but it may be called out also by excitation of distant afferent nerves.

If these reflex effects are not confined within too small a vascular field, they influence the general blood pressure.

Since in almost every afferent stimulation, vessels somewhere are constricted and others dilated, it is evident that changes of pressure may take place in both the positive and the negative direction.

As a rule, *afferent excitation* produces a reflex rise of pressure (Fig. 97). Under certain circumstances a fall is obtained instead, for example: when the afferent nerve stimulated is subjected to the cold; when after having been sectioned it is allowed to regenerate to a certain stage; if the stimulus is weak.

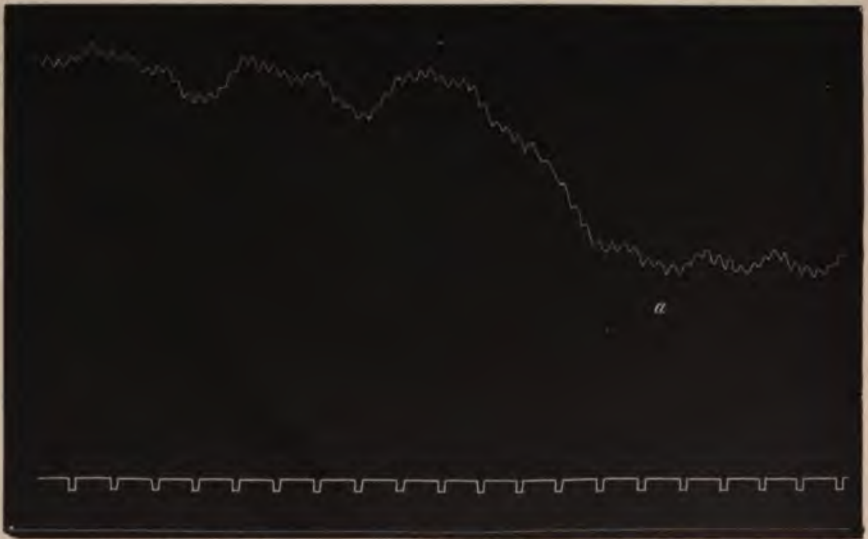

FIG. 97.—Reflex rise of blood pressure in the rabbit (to be read from right to left). At *a* the skin was stimulated.

At present it is impossible to decide whether these different reflexes are caused by two kinds of efferent nerves or by the difference in behavior of the vasomotor center to stimuli of different strength. There are nerves however which, so far as our present information goes, *mediate only a fall of pressure,* whatever the strength of stimulus. Such a nerve is the depressor, already mentioned at page 193. The afferent nerves from the muscles have the same influence on the blood pressure (Fig. 98).

The *reflex fall* of pressure on stimulation of the depressor appears *with both vagi cut*; hence, it is independent of changes in the heart frequency and is caused essentially by a vasodilation. This involves primarily the region of the abdominal cavity innervated by the splanchnics, although *other parts of the body* may take part in it.

The *reflex rise* of pressure is produced *primarily* by a contraction of the vascular region innervated by the splanchnics, even though other regions also may be concerned. Not all the vascular regions of the body are constricted, at least not to the same extent, when the pressure rises; for vasodilatation has often been observed in different organs, especially in the muscles.

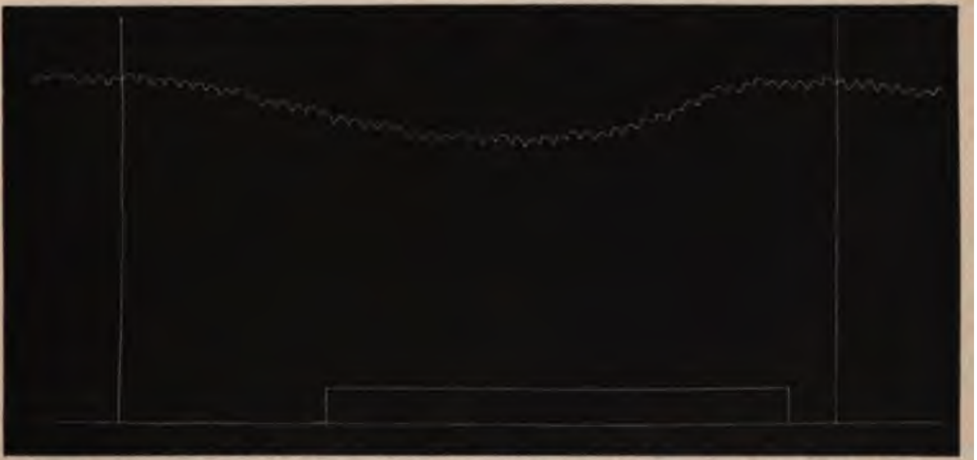

FIG. 98.—Reflex fall of blood pressure in the rabbit produced by stimulation of an afferent muscular nerve (to be read from right to left). The period of stimulation is indicated by the vertical lines. |‾‾‾‾‾‾‾| = ten seconds.

It is difficult to decide in many cases whether a given dilator effect is active or passive. It may be that with an increase of pressure produced by an extensive contraction of the splanchnic region, various other regions dilate only because of the high pressure. Or it may be that dilatation is actively produced, either by a decline in the tonus of the constrictor nerves or by stimulation of the dilator nerves.

A fall in pressure obtained reflexly is caused by a reduction of tonus in some of the great vascular regions. But as in the case of a rise of pressure, the reduction may be due either to stimulation of dilator nerves, or to diminished activity of the constrictors. After excluding all the vasoconstrictor nerves of the hind limb, Bayliss succeeded in demonstrating vasodilatation in the same region by stimulation of the vagus. In this case, therefore, the dilatation took place through the *activity* of the vasodilator nerves.

§ 12. THE VASOMOTOR CENTERS

We have no positive data as yet for the location of *centers for the vasodilator nerves.* These nerves have been followed far into the central nervous system, and it is very probable that their chief center, like the centers of the other vegetative functions, lies in the medulla oblongata.

The chief *center for the vasoconstrictor nerves* is positively known to lie in the medulla. In the rabbit it occupies on each side a small prismatic space; in man in a cross section taken at the level at which the facial nerve passes off, it appears as one or more aggregations of gray matter on the median side of the facial tract. From this center the vasoconstrictor nerves descend chiefly, but not exclusively, in direct paths along the cord and pass out in the nerve roots already mentioned (page 232). As we have seen, the center is under tonic stimulation. If by *transecting the cord*, its influence be cut off, the vascular tonus falls and as a consequence the blood pressure becomes considerably less.

But the vascular tonus is *not entirely obliterated* by this operation. On the contrary, it has been shown that throughout the entire length of the *spinal cord*, with the exception only of the cervical region, and the lowest part of the lumbar, there are centers for the vasoconstrictor nerves which can be stimulated both reflexly and by asphyxiation. These centers appear to be less excitable than the vasomotor center in the medulla (although this is denied). They do not react so promptly as that center; but their activity lasts longer; and in virtue of their greater endurance they appear to be of no less importance for the maintenance of vascular tonus.

Experiment has shown also that *after destruction of a large part of the spinal cord*, the tonus of the vessel may be gradually restored. The vessels which receive their constrictor nerves from the destroyed part of the spinal cord are at first entirely paralyzed, and they are dilated to their maximal extent. But gradually their tonus returns; they react to local application of cold and heat much the same as in the normal condition, but are not influenced by distant parts of the body (Goltz and Ewald). Either the *vascular wall* itself must have the property of contracting in a tonic manner, when it is entirely isolated from the central nervous system, or this tonic contraction is caused by *ganglion cells* strewn along the peripheral course of the vasomotor nerves, which then serve as vasomotor centers of a third order. A definite decision between these two alternatives is not possible, and the inherent probability of the one or the other naturally shapes itself according to one's inclination to ascribe greater or less importance to the peripheral ganglia.

The fact remains however that vessels entirely isolated from the central nervous system can recover their tonus. And the action of the vasodilator nerves favors the idea that vascular tonus is, at least in part, of peripheral origin. We know of no muscles whose contraction could cause the vessels to dilate. Dilatation must be caused therefore by *diminishing the activity of the circular muscle fibers*—i. e., vasodilator nerves must be a kind of *inhibitory nerves*. They can even exercise their characteristic influence upon the vessels when all the vasoconstrictor nerves to the same part of the body have been cut. In other words, a certain tonus of the vessels remains after section of the constrictor nerves, which however is entirely obliterated by stimulation of the vasodilator nerves.

We can form the following conception, therefore, of the innervation of the blood vessels. The musculature of the vessels is under the influence of the *central nervous system and of peripheral structures*. In the former is found the vasomotor center located in the medulla, which constitutes the *chief center* of the vasoconstrictor nerves. The centers distributed in the spinal cord represent *centers of the second order,* and the peripheral ganglia or the musculature of the vessels, as the case may be, represent *centers of the third order.* The last named can exert a powerful influence even when they are isolated from the others. As a rule, the musculature of the vessels is in a *state of tonic contraction* because of impulses passing out over this chainlike series of centers. The contraction is more or less weakened by stimulation of the vasodilator nerves, since they exert an inhibitory influence on the peripheral mechanism.

The parts of the brain above the medulla, especially the motor zone of the cerebrum, influence the blood vessels. With regard to this influence, I believe with Fr. Franck that it is to be conceived in the same way as that produced by the same parts upon the cardiac nerves—i. e., that the vasomotor center of the medulla is set in action by these parts of the brain in exactly the same way as it is stimulated by the other parts of the body through their afferent nerves. And just as we have seen that in muscular activity the acceleration of the heart is conditioned by this influence of the cerebrum upon the medulla, we may infer from the facts which we already have that the change in vascular tonus taking place in muscular work are produced by a similar influence.

§ 13. GENERAL CONSIDERATIONS ON THE DISTRIBUTION OF BLOOD IN THE BODY

The distribution of blood in the body depends partly upon mechanical conditions, but chiefly upon the vasomotor nerves.

A. MECHANICAL IMFLUENCES

To these belong first the caliber of the afferent arteries; the greater the caliber, the greater, other things being equal, must be the supply of blood to the part. Moreover the *attitude of the body* plays a prominent part especially in the flow of blood in the veins. In the upright position, for example, the veins of the lower extremities are dilated because of the hydrostatic pressure of the blood column, and they contain a large quantity of blood. In changing to the horizontal position the rich supply of blood to the lower extremities decreases. The quantity which is shifted in this way amounts in a grown man to about 100 g. (Mosso).

The influence of the respiratory movements on the circulation has already been discussed. With a positive pressure in the thoracic cavity, for example, in severe muscular effort, when the lungs are inflated and the glottis is closed, the return flow of blood to the heart is hindered and the quantity in the extremities increases.

If with the body in a vertical position, the head being upward, the splanchnics be cut so as to paralyze the great vascular region of the abdominal viscera, and the respiration be then interrupted, the circulation stops at once. The dilated vessels of the abdomen contain so much blood that the heart no longer receives a sufficient supply. In such cases, however, the circulation can be restored to some extent by respiratory movements, the blood being drawn by the aspiration of the thorax from the venæ cavæ to the heart (Hill and Barnard).

An increase or decrease of turgor in a certain part incident to different positions of the body must evidently produce in other parts changes of an opposite character. The volume of one arm is greater when the other is held passively above the head; the volume of the hand increases when both femoral arteries are compressed, etc. Reflex activity of the vasomotor nerves often comes in here to influence the result.

B. THE INFLUENCE OF VASOMOTOR NERVES

In general one may say that *under normal circumstances* every part of the body *receives exactly as much blood as it has need of,* and that by dilatation of vessels a particular part receives *more blood the more active it is.* At the same time blood vessels in other parts of the body are constricted, and in this way the normal blood pressure necessary for life is maintained by an incessant reciprocity between the different vascular regions.

In the state of bodily rest the organs of the *thorax* and *abdomen* contain a relatively large part, as a rule *more than half,* of the total quantity of blood in the body. The content of blood in these organs amounts to about twenty per cent of their weight, while the blood content of the skin, skeleton, muscles and the nervous substances amounts to only two to three per cent of their weight (Ranke *et al.*). The blood stored up in the internal organs is always at the disposal of any organ which has need of a larger supply.

Thus in muscular work the vessels of the muscles and skin are dilated, while at the same time the vessels innervated by the splanchnic nerve are constricted to a greater extent. Consequently the blood pressure as a rule, if not always, increases.

By the use of apparatus constructed for the purpose of determining the velocity of the blood, the quantity flowing through some of the organs in a given time has been measured directly (cf. also page 211). In the dog Tschuewsky found the quantity per minute and per 100 g. of organ to be 3.4 c.c. for the hind limbs with the nerves intact, and 9.9 c.c. after section of the nerves. The head received 16.6 c.c., muscles with uncut nerves 13 c.c., the thyroid gland 590.9 c.c. (!), all per minute and per 100 g. of organ.

In the researches of Chauveau and Kaufmann the quantity of blood flowing through the levator superiorus proprius muscle of the horse was: in rest, on the average, 17.5 c.c. per 100 g.; in activity, it rose to 85 c.c. According to Bohr and Henriques, the dog's heart receives on the average 30 c.c. per minute per 100 g.

In view of its function of removing from the body the nitrogenous products of metabolism, the kidney receives a relatively large quantity of blood, especially if great demands are made upon it by transfusion of a diuretic agent (cf. Chapter XIII). There then flows through the kidney (dog) per minute a quantity of blood which amounts to one hundred and forty per cent of its own weight (average ninety-six per cent). In the same animal the quantity of blood expelled from the left heart per minute may be estimated at about ten per cent of the body weight. Hence, in strong diuresis the blood supply to the kidney would be *relatively fourteen times as great as to all the organs taken together.*

Furthermore the distribution of blood to the different parts of the body exhibits incessant fluctuations produced by the vasomotor nerves, which are connected either with the activity of the organs, or with the heat regulation of the body; for the heat regulation is controlled in the main by vasomotor nerves (cf. Chapter XIV).

The *blood flow to the brain* calls for a special discussion. In the *child* while the skull is not yet completely ossified, the great fontanel exhibits pulsations which are undoubtedly caused by the heart beats and by the respiratory movements, and which show moreover that the blood supply to the brain may vary under different circumstances.

How far this is true in the *mature, uninjured skull* has been much debated. Were the skull cavity rigidly closed on all sides, and were the brain substance nearly incompressible, the same quantity of blood should be present in the brain at all times. But this would not be true, if water or other material were secreted from the blood vessels or otherwise extravasated; for then the quantity of blood equivalent to the volume of material poured out of the vessels would be displaced. Otherwise blood flowing away by the veins would always make room for the blood flowing in by the arteries.

But it has been shown that this conclusion is not strictly correct, and that *the quantity of blood in the brain can in fact increase and decrease.* The skull cavity is not surrounded on all sides by solid bony walls. It communicates with the spinal canal, between the inner surface of which and the outer surface of the dural sac are numerous venous plexuses connected with the veins of the general system. The foramina intervertebralia are filled with a vacuolated tissue, which can be pressed outward. The subdural space communicates with the deep lymph vessels and glands of the neck, as well as with the lymph tracts of the peripheral nerves.

The subarachnoid spaces are likewise in connection with the lymph tracts of the peripheral nerves. The cerebrospinal canal therefore must be regarded as a rigid-walled cavity with an elastic door.

Now it has been found both by experiments on animals, and by physical (Grashey) and mathematical (Lewy) calculations, that the *regulation of the blood flow to the brain* takes place in exactly the same way as in the other organs—i. e., dilatation of the arteries produces an increase in the flow, constriction a diminution. Any stasis of venous blood causes an arterial anæmia, just as does a severe compression, as for example by a foreign body forced into the skull cavity. So long, therefore, as it is a question only of the alterations in arterial volume, which correspond to the physiological needs, the circumstance that the brain is inclosed by a solid, unyielding capsule is of no essential importance.

Jensen has found that the quantity of blood flowing to the brain of a rabbit is on the average 136 c.c. per 100 g. per minute (extremes 60–278 c.c.). In the dog he found as a mean of two researches 138 cc. The *brain receives relatively more blood than any of the other organs thus far studied except the thyroid gland.*

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CHAPTER VII

DIGESTION

THE purpose of digestion is to so change the foodstuffs that they can pass into the blood and be utilized in metabolism. To this end the food is subjected to mechanical division and chemical transformation in the digestive organs.

Of all the combustible constituents of our diet, only sugar is soluble in water. Starch and coagulated proteid are insoluble in water; but by digestion they are so changed that they can be taken into solution. Fat also, which is insoluble in water, is transformed so that it can be absorbed from the alimentary tract into the blood.

The organic foodstuffs, which are already soluble, undergo transformations in the alimentary canal which adapt them to the requirements of metabolism. The noncombustible constituents of the diet, water and the salts, do not require to be digested in order to be taken into the blood.

In man the work of the digestive system is materially aided by the preparation of "dishes" of food, since the foodstuffs are thereby rendered more easily accessible to the digestive fluids.

The heat necessary to boil or roast meat swells the connective tissue, which holds the muscle fibers together, and changes it partly into gelatin. The meat at the same time becomes less compact, and so is the more readily reduced to fine bits by our teeth. In the cooking of vegetable foods, the cell membranes are ruptured by the heat and the starch granules are transformed into a soluble modification. In bread baking the dough is rendered spongy by the carbon dioxide formed in "raising," and this is carried still further by the heat of the oven, by which also the starch granules are transformed in the same way as in ordinary cooking.

FIRST SECTION

THE DIGESTIVE FLUIDS

§ 1. GENERAL SURVEY

The fluids secreted by the digestive glands serve either to change the chemical nature of the foodstuffs so that they shall be fit for absorption, or they aid the processes going on in the alimentary canal in some other way. Certain products also which are given off with the digestive fluids are destined merely to be eliminated from the body. In this section we shall consider in the main only the constituents important in digestion.

In order to study the chemical properties and the action of the different digestive fluids, one may use either extracts of the appropriate glands or the natural secretion collected from their ducts. In the latter case the duct is shifted from its normal connections and is made to open as a fistula on the outer surface of the body, so that it conveys the secretion to the exterior.

The first *fistula* of a digestive gland to be the subject of a thoroughly scientific investigation was one resulting from a gunshot wound in the stomach of a Canadian hunter. As a consequence of his accident, the hunter had all the rest of his life a stomach fistula opening at the upper part of the abdomen, through which the interior of the stomach could be observed and gastric juice could be obtained. From observations on this man extending over a number of years (1825–1833) Beaumont collected a large number of important facts concerning the digestive process in the stomach, and concerning the movements of that organ. Later Bassow and Blondlot (1842) showed how a stomach fistula may be made on an animal. Since that time such fistulæ have been made for therapeutic purposes on man himself, and they have been used to good advantage for the study of gastric digestion.

The *pancreatic juice* is obtained by means of a cannula fastened in the duct of Wirsung, or from the open duct sutured to the abdominal wall, or finally by isolating that portion of the intestine into which the duct opens and bringing it forward to the abdominal wall.

In order to study the secretion of *bile*, fistulæ are made in the gall bladder. The ductus choledochus can be tied off and the bile can thus be entirely shut out of the intestine, or the duct can be left open, so that the bile flows as usual to the intestine except when the fistula is open (amphibolous biliary fistula). The intestinal loop containing the mouth of the duct can also be resected and brought forward to the abdominal wall. By the last method especially it is possible to observe how the bile flow is affected by different kinds of food.

To obtain pure *intestinal juice* a loop of the intestine is isolated, one end of it is sutured to the skin and the other is closed (Thiry's fistula); or both ends may be sutured to the skin (Vella's fistula), in which case the intestine is of course more accessible.

The most important constituents of the digestive fluids are certain enzymes which may be classified in three groups: proteid dissolving (*proteolytic*), sugar forming (*diastatic* or *amylolytic*) and fat splitting (*lipolytic*). All of the digestive enzymotic processes agree in this, that the organic foodstuffs acted upon absorb the constituents of water and are split into simpler compounds (hydrolytic cleavage).

The enzymes are formed in the different glands of the alimentary canal; namely, the proteolytic in the glands of the stomach and in the pancreas; amylolytic in the salivary glands, in the pancreas and in the glands of Lieberkühn of the small intestine, lipolytic in the mucous membrane of the stomach and in the pancreas.

Two enzymes which act on the same foodstuffs are not necessarily identical. For example, pepsin from the gastric glands acts on proteid in an acid medium, while trypsin from the pancreas acts on proteid in neutral and alkaline media.

The enzymes are, so far as we know, formed in the glands themselves. During the intervals between meals they are deposited in the glands, to be poured out when required for digestion. But we do not find the finished product in the glands: instead, precursors of the enzymes, the so-called *zymogens*, are elaborated in them and are transformed into the enzymes either during the act of secretion or in the secretory product after it is given off (Fig. 99).

Artificial digestion is often employed in studying the action of the digestive fluids on the foodstuffs—i. e., a given food is mixed either with the fluid secreted by a gland or with an extract of the gland, and the mixture is kept for a time at body temperature. A great mass of important facts has been obtained in this way; but we cannot apply the results of artificial digestion to the natural process in the body without some reservation. For, even neglecting the mechanical work of the alimentary canal, there are several important differences between the two. (1) In natural digestion the fluid is always adapted in quantity and quality to the quantity and character of the food acted upon, while in artificial digestion both the quantity and the character are fixed for a given experiment. (2) In the natural process the products of digestion are removed by absorption as soon as they are formed; in artificial digestion they remain in the mixture. This is of no small consequence; for in the one case the course of digestion is affected by the presence of these products (cf. page 38), while in the other this is prevented by their prompt removal from the sphere of action. (3) Finally, in the normal course of digestion the different secretions may influence each other so that the final result may be essentially modified.

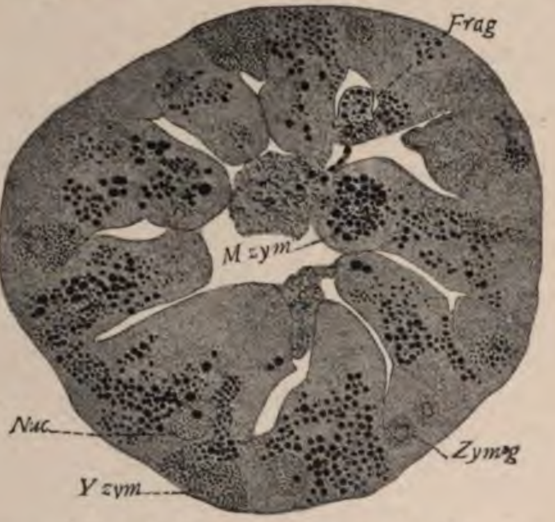

FIG. 99.—Transverse section of the hepato-pancreas of an isopod crustacean, fixed in osmic acid, showing the gradual transformation of zymogen granules into secretion droplets, after Murlin. The zymogen granules appear first immediately about the nucleus (*Zym'g.*). As the cell grows in size the granules increase in number so as to almost fill the cell (*Y. zym.*). Still later they absorb fluid from the protoplasm and swell up, being finally discharged from the free border of the cell as secretion droplets (*M. zym.*). *Frag.*, fragment of a cell broken off and lying in the lumen of the gland; *Nuc.*, nucleus of a mature cell.

Mett employs the following method of determining the strength of a proteolytic enzyme in a digestive fluid. Fresh white of egg is sucked into a narrow glass tube, the tube is dipped into water at 95° and is then allowed to cool slowly. The tube is now broken into small pieces and one of them is placed in the fluid to be tested. The number of millimeters of the coagulated albumin dissolved in a unit of time affords a measure of the enzymotic action. Amylolytic action can be determined in a similar way by means of tubes containing colored starch paste, and lipolytic action by finding the amount of fatty acids set free in a given time from a known quantity of neutral fat.

§ 2. SALIVA

Saliva is secreted by the three pairs of large salivary glands located in the neighborhood of the buccal cavity and opening into it by their several ducts, and also by small glands embedded in the mucous membrane of the mouth.

The product has a varying constitution according to the gland by which it is formed, and on the basis of the characteristic properties of their secretions the salivary glands may be divided into two chief groups. One group, called *albuminous glands,* produce a thin, watery secretion, which contains only proteids, salts, and in certain cases a diastatic enzyme. Here belong the parotid gland of all mammals, the submaxillary of the rabbit, some of the glands in the nose and tongue, and the lachrymal glands. The other group—the *mucous glands*—secrete a more or less viscid fluid, which contains *mucin* as its characteristic ingredient, besides salts and small quantities of proteid. This group includes the submaxillary glands (with few exceptions), the sublingual, part of the buccal glands, those in the mucous membrane of the pharynx, the larynx, trachea and œsophagus. There are also *mixed glands*—e. g., the submaxillary of man—in which a part of the gland conforms to one of these types, and a part to the other.

The *mixed saliva* of man is a colorless or light-bluish, turbid, odorless, slippery and viscid fluid, which upon standing for a time separates into an upper, transparent and a lower, turbid layer, the latter consisting of mucous flakes, salivary corpuscles, epithelial scales from the mouth, etc. The reaction as a usual thing is weakly alkaline although it may be neutral, or even weakly acid. It is asserted that the reaction early in the morning is weakly acid, neutral or amphoteric, that after every meal it becomes alkaline and then gradually returns to the neutral or weakly acid reaction. The specific gravity is 1.002–1.009.

The chief constituents of mixed saliva are: proteid, mucin, a diastatic enzyme (ptyalin), and potassium sulphocyanide (KCNS).[1] Besides, we find inorganic salts, gases and traces of ammonia, nitrous acid, urea, etc. Certain drugs also are removed from the blood in the salivary secretion.

According to recent analyses, the human saliva contains 98.8–99.5 per cent water, and 0.5–0.2 per cent solids of which 0.1–0.4 per cent is organic; the salt content is 0.1–0.2 per cent and the KCNS, 0.003–0.01 per cent. The quantity of mixed human saliva secreted in twenty-four hours is about 1,500 c.c.

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[1] We can only say with regard to this substance that its N and S probably come from proteid. It has been assumed to confer an antiseptic action on the saliva, but this is not confirmed.

The Diastatic Enzyme.—In 1831 Leuchs found that saliva gradually dissolves starch and converts it into the soluble carbohydrates, dextrin and sugar. This action is to be ascribed to an enzyme, called *ptyalin.*

Dry starch is not soluble, but it swells up in warm water, forming starch paste. On heating starch with glycerin up to 190°, or by acid fermentation of the paste, it is rendered soluble. Soluble starch is also the first product of digestion under the action of ptyalin. In the further course of this action soluble starch is split by absorption of water into dextrin, isomaltose, and maltose. There is present in saliva a trace of an inverting enzyme, maltase,[1] which converts a small quantity of maltose into dextrose (Röhmann).

More in detail, this transformation of starch into sugar proceeds about as follows: First the soluble starch is split into *erythrodextrin* (red color with iodine) and maltose. Then from the erythrodextrin is formed an *achroodextrin* (no color with iodine) and more maltose, and achroödextrin in its turn yields another *achroödextrin* and more sugar, etc.

In artificial digestion starch can never be completely changed into sugar. But if the experiment be so arranged that the sugar can be removed by dialysis as it is formed, the transformation may be carried much farther than is possible otherwise (Lea). Since provision for removal of the sugar is made in the digestive system, it is probable that all the starch is transformed, provided only that the ptyalin has the opportunity of acting long enough.

Human saliva acts very rapidly. When equal volumes of saliva and starch paste are mixed, at body temperature the starch disappears in about two and a half hours. Cooked starch is digested more rapidly than raw, and pulverized starch more rapidly than nonpulverized.

Ptyalin appears to act more powerfully in a *neutral* or *weakly acid medium*; hence best results are obtained when the alkaline saliva is carefully neutralized by addition of a very small quantity of acid (not more than 0.0007–0.0012 per cent HCl; Cole).

§ 3. GASTRIC JUICE

Gastric juice cannot be obtained pure from an ordinary gastric fistula, for even if the particles of food could be excluded, it would be mixed with some saliva which had been swallowed. In the dog, however, these difficulties can be overcome, by making both a stomach fistula and an œsophageal fistula (Pawlow). The stomach can also be cut off from both œsophagus and duodenum, the latter two sutured together, and the juice collected from the isolated stomach (Fremont).

Gastric juice obtained in this way, when it is freed from the stomach mucus, is perfectly clear in color, acid in reaction and is devoid of foreign taste. Its specific gravity is 1.003–1.0039. In a layer 20 cm. long it rotates the plane of polarized light 0.70°–0.73° to the left. Its dry residue amounts to 0.29–0.60 per cent, the ash to 0.10–0.17 per cent. It contains neither peptone, nor leucin, nor tyrosin, but always contains proteid, and at times traces of fatty acids. At a low temperature it becomes turbid, and separates into three layers: an upper clear layer, a median turbid layer, and a lower one consisting of a sediment of small, homogeneous, strongly refractive granules.

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[1] In general the enzymes are named by adding the suffix *ase* to the name of the substance on which it acts. Exceptions to this rule are older names still in use.

The analysis by Schumow-Simanowsky of the pure gastric juice of the dog is as follows:

Acid	0.46 –0.58 per cent.
Chlorine	0.49 –0.62 "
Dry residue	0.43 –0.60 "
Ash	0.09 –0.16 "
Coagulation by alcohol	0.14 –0.19 "
Coagulation by heat	0.13 –0.18 "
Precipitation at 0° C.	0.011–0.003 "
Phosphoric acid	0.004 "

Gastric juice inverts cane sugar, digests proteid, gelatin and gelatin-forming substances, coagulates milk and splits emulsified fats into fatty acid and glycerin.

The inversion of cane sugar is accomplished by the acid, the digestion of proteid, etc., by *pepsin,* the coagulation of milk by *rennin,* the cleavage of emulsified fats probably by a third enzyme, the *gastric steapsin.* We have now to study more closely the acid and these enzymes of the gastric juice.

A. THE ACID OF THE GASTRIC JUICE

Proof was given by Prout as early as 1844 that the acid reaction of the gastric juice is due to free HCl [1]; but it was not incontestably established until C. Schmidt (1852) by his convincing analyses showed that more chlorine is secreted by the mucous membrane of the stomach than can unite with all the inorganic bases, including ammonia, present in the gastric juice.

The percentage of HCl in the gastric juice is very different in different animals. In the dog it amounts to 0.46–0.58 per cent; and in the case of a boy with a complete œsophageal stricture and a stomach fistula, it was found to be 0.39–0.57 per cent. In other fistulous patients 0.05–0.3 per cent has been observed.

When proteids are taken into the stomach, the HCl unites with them, and later with the products of their digestion (Sjöquist). On this account and because the HCl reacts with the phosphates of the food with liberation of phosphoric acid, great difficulty is experienced in determining the quantity of HCl in the stomach contents, and in following its quantitative variations. Nevertheless, the mucous membrane secretes more acid than is necessary to combine with the proteid, consequently free acid can always be demonstrated, at least in certain stages of digestion.

The HCl combined with proteids seems to insure their digestion; the conception that only free acid could be of importance is therefore not sound.

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[1] Lactic acid found in the stomach is probably formed by bacterial decomposition of carbohydrates.

B. PEPSIN

After Spallanzani (about 1780) had shown that the gastric juice can produce chemical changes outside the body, Eberle (1834) was the first to demonstrate the same effects with extracts of the gastric mucosa, and Schwann (1836) pointed out that a substance formed in the mucosa, which he named *pepsin,* is involved in this action.

Under this name is described the enzyme which acts in acid medium upon proteid, gelatin and connective tissues, causing them to absorb water and to split into simpler compounds. Pepsin has no effect in neutral solution, and is destroyed in soda solution.

From pure gastric juice of the dog, Nencki and Sieber, also Pekelharing, have prepared by dialysis a very pure pepsin. This is a proteid body, containing 51–52 per cent C, 6.7–7.1 per cent H, 14.4 per cent N, 1.5–1.6 per cent S, and 0.5 per cent Cl. and some Fe. On cleavage it yields a pentose, purin bases, and an acid (pepsinic acid, 50.8 per cent C, 7.0 per cent H, 14.4 per cent N, 1.1 per cent S). Since in a strongly active preparation no trace of phosphorus could be demonstrated, pepsin cannot be numbered among the nucleoproteids. On the other hand, it is possible that it unites with lecithin to form a compound analogous to jecorin (page 79).

Pepsin occurs in the mucous membrane only in the preliminary form of its zymogen, *pepsinogen.* We have seen that pepsin is destroyed by soda. If however the mucous membrane be extracted with a *weak* soda solution and the extract be then acidified with HCl, a pepsin-containing fluid of good digestive properties is obtained (Langley). Therefore there must be in the mucosa a substance which is not destroyed by soda, and which is transformed into pepsin by treatment with acids.

In artificial digestion the quantitative results depend upon the following factors: temperature; the amount of pepsin; the amount and the kind of acid; the kind and the amount of proteid; the presence of the products of digestion; and the presence of certain inorganic salts.

The quantity of enzyme necessary to produce a very powerful digestive action is very small. Thus in a certain artificial gastric juice of very excellent digestive power, there was found for example only 0.067 per cent of nonvolatile organic matter.

If, however, the quantity of HCl and of proteid remaining the same, the quantity of pepsin be increased, the rate of digestion is increased, so that up to a certain limit the action is proportional to the square root of the concentration of the enzyme (Schütz). The same law holds also for the enzymes contained in the pancreatic secretion (Walther).

The acidity of the digest is a matter of particular importance. We find: (1) that the optimum acidity is very different for different proteids; (2) that too much or too little acid stops all digestive action. The most powerful action on fibrin, for example, is said to be obtained with an acidity of 0.09 per cent HCl; at 0.13 per cent and 0.02 per cent the action is very feeble. But on coagulated white of egg the best effect is obtained with 0.16–0.25 per cent HCl.

In the transformation of proteid under the influence of pepsin a number of different substances arise by cleavage, the composition of which becomes simpler and simpler the farther the cleavage progresses.

These substances may be separated one from another by fractional precipitation with ammonium sulphate. Those precipitated by a degree of saturation of twenty-four to forty-two per cent are called primary *albumoses* (*heteroalbumose, protoalbumose*). Those precipitated by stronger concentration of the sulphate are designated *deuteroalbumoses.* Those easily diffusible products not precipitated by the salt, but still giving the biuret reaction, are known as *peptones.* After acidification of the solution the peptones, in an impure condition, can be separated from other end products by precipitation with picric acid.

We have then from peptic cleavage of proteid (besides acid albuminate) first, two *primary albumoses* (hetero- and protoalbumose), and then *deuteroalbumose* (Pick, Zunz). Primary albumoses show a higher percentage of C and N and a lower percentage of O than the original proteid (e. g., in fibrin, there are 52.7 per cent C, 16.9 per cent N, 1.1 per cent S, and 22.5 per cent O, while in the primary albumoses derived from it we find 55.4 per cent C, 17.8 per cent N, 1.2 per cent S, and 19.1–18.7 per cent O). Heteroalbumose from fibrin contains thirty-nine per cent of the total nitrogen in basic form and fifty-seven per cent as monoamino acids, while the corresponding numbers for protoalbumose are twenty-five and sixty-eight per cent respectively. Heteroalbumose contains only a small quantity of the aromatic groups which yield tyrosin and indol, but it is rich in those groups which yield leucin and glycocoll. Protoalbumose, on the other hand, yields abundance of tyrosin, indol and skatol, but only a little leucin and no glycocoll.

The third direct product of digestion is a *deuteroalbumose* (*synalbumose*) which is characterized chiefly by the fact that it contains a carbohydrate group, whenever such a group occurs in the parent proteid molecule. Its quantitative composition differs materially from that of the primary albumoses: thus 48.7 per cent C, 13.8 per cent N, 30.5 per cent $S + O$.

On further cleavage with pepsin, primary albumoses yield *secondary albumoses* which appear to be very numerous. Among them *thioalbumose* should be especially mentioned on account of its high content of S (three per cent).

Deuteroalbumoses are transformed into *peptones*, the molecular weight of which is relatively small—only about 500 by the depression of the freezing point, whereas the molecular weight of deuteroalbumose is about 3,200.

According to Kühne, peptic cleavage of proteid could proceed only as far as the formation of peptones. Later it was found that from the beginning of the cleavage, substances separate off which no longer give the biuret reaction. Among these are certain intermediary substances, the *peptoids*, comparable in their structure to the peptones, from which after long-continued digestion the end products finally appear. Probably all of the *hydrolytic cleavage products* (cf. page 72) belong here, for already the following have been demonstrated in such digestive mixtures: leucin, asparatic acid, cadaverin, putrescin, glutamic acid, tyrosin, amino-valerianic acid, dihexosamin, lysin, penta-methyl-endiamin, phenylalanin, cystin, α-pyrrolidin-carboxylic acid, tryptophan (Pfaundler, Lawrow, Langstein, Salaskin, Fischer, and Abderhalden).

The relative proportion of primary digestive products obtained fr
ferent kinds of proteids is very different. The kind of albu

likewise very different, though they are all included under the common name *proteoses*. The glutin-forming substances are changed by gastric juice into gelatin, and this into gelatin peptones.

The same decompositions which proteids suffer in digestion they exhibit also when treated with acids or alkalies or superheated steam, and when they fall under the influence of putrefactive Bacteria. In fact, weak salt solutions have a digestive action on proteids (Dastre). The action of the enzymes is not to be regarded, therefore, as particularly exceptional.

Loss of the power of coagulation on the part of the blood and other harmful effects which have long been known to follow intravenous injection of albumoses have lately been attributed to other substances—e. g., *peptozymes*—mixed with them (Pick and Spiro). Peptozymes, acting mainly in the liver, cause the production of a substance which prevents coagulation (Contejean, Gley).

C. RENNIN

It has long been known that milk coagulates by precipitation of its casein when it comes in contact with the mucous membrane itself, or is mixed with an extract of the membrane. Since acids produce the same effect it was supposed that this precipitation was due to the acid reaction of the mucosa. But the investigations of Selmi and Heinz, and especially those of Hammarsten (1872) and of Alex. Schmidt showed that coagulation takes place in a neutral or alkaline reaction, that the acid is, therefore, quite superfluous, and finally that coagulation of milk is effected by a special enzyme called *rennin* or *chymosin*.

Rennin occurs in the mucous membrane as a precursor, *rennin-zymogen,* which like pepsinogen is more resistant to alkalies than its enzyme, can be extracted from the mucosa with water, and is transformed into the active enzyme by addition of acids. In its action rennin resembles the other digestive enzymes. One part of the impure enzyme can coagulate 400,000 to 800,000 parts of casein.

In the coagulation of milk produced by rennin, casein first suffers cleavage into paracasein, and whey proteid, a substance resembling albumose; the former, which is the chief product, then precipitates out in solid form, provided Ca salts are present in the solution. If Ca salts are absent, cleavage occurs under the influence of rennin, but no coagulation.

D. GASTRIC STEAPSIN

After Marcet, Cash and Ogata had demonstrated the decomposition of neutral fat in the stomach, Volhard made further investigations on the subject and established this property of gastric juice beyond doubt—with the limitation, however, that it acts only on emulsified fats, but on these very powerfully.

The rule holds for stomach steapsin, as for other enzymes, that its action is proportional to the square root of concentration. It is quickly destroyed in a strongly acid gastric juice. The pure pepsin of Pekelharing has no fat-splitting action, a fact which speaks decisively for the independence of the gastric steapsin.

§ 4. PANCREATIC JUICE

Pancreatic juice presents different properties according as it is obtained from a long-established fistula or a recent one (page 243). In the latter case it is viscid or almost ropy, and at a low temperature passes over into a transparent jelly from which a thin fluid separates out. At 0° C. there is formed a gelatinous, flocculent precipitate, readily soluble in dilute acids. Under some circumstances the secretion is so rich in proteid that the whole fluid coagulates when heated. The secretion from a permanent fistula is thinner and contains a smaller quantity of solids.

According to Pawlow the latter is to be regarded as the normal secretion. In his experience the thick, sirupy secretion is due to the effects of the operation on this uncommonly sensitive gland.

The quantity of pancreatic juice secreted daily is no more to be estimated with exactness than is the quantity of gastric juice. In cases of pancreatic fistula in man a daily secretion of from 293 to 840 c.c., with an average of something more than 400 c.c., has been observed.

Pancreatic juice is always alkaline in reaction and often contains an abundance of proteid as the following analyses show:

	Dog (Zawadsky).	Man (Glaessner).
Dry residue	13.59 per cent.	1.25–1.27 per cent.
Organic substance	13.25 "	0.50–0.54 "
Proteid	9.21 "	0.13–0.17 "
Ash	0.34 "	0.57–0.70 "

Kudrewetsky has found that the alkalinity as determined by the quantity of HCl in g. necessary to neutralize 100 c.c. of dog's pancreatic juice is 0.05–0.89.

Its most important constituents are the enzymes: two or three amylolytic, one proteolytic and one lipolytic. Probably all of these occur in the gland as zymogens. That they are actually different enzymes probably follows from the fact that the amylolytic, proteolytic and lipolytic effects either of the secretion or of the pancreatic extract do not keep pace one with another.

A. THE AMYLOLYTIC ENZYMES

Valentin (1844), also Bouchardat and Sandras (1846) found that pancreatic secretion transforms starch into sugar. The very same cleavages appear in this as in the action of ptyalin on starch. Besides, pancreatic juice contains an enzyme (*maltase*) which changes maltose to dextrose (Röhmann) and according to Weinland, another (*lactase*) which splits milk sugar into dextrose and galactose.

Glaessner was unable to demonstrate any action of human pancreatic juice on cane sugar, maltose or milk sugar.

The action of the amylolytic enzyme is favored by small quantities of hydrochloric acid and of bile (Rachford).

B. THE PROTEOLYTIC ENZYME, TRYPSIN,

is distinguished from pepsin mainly by the fact that it digests proteids in an alkaline medium. Purkinje and Pappenheim as early as 1836, and Cl. Bernard later alluded to the proteolytic action of the pancreatic juice, but Corvisart (1857) must be looked upon as its real discoverer. Later Kühne, especially, did large service for our knowledge of this enzyme.

Trypsin as such does not occur in the pancreas, but instead a zymogen, which, like those of the other enzymes, is more resistant toward all kinds of injurious agents than the enzyme itself. But even the secreted juice does not contain any trypsin and is entirely without effect on proteid, if it is not first activated by an enzyme, called *enterokinase* (Pawlow), found in the intestinal juice. The formation of trypsin from its zymogen presupposes therefore the presence of this special enzyme, and according to Delezenne, Popielski, Bayliss and Starling, there is no other means of bringing about this change. (The unactivated secretion, nevertheless, will digest boiled fibrin and casein, though very slowly.)

Opposed to these observations however are others according to which a powerfully active extract is obtained, if, for example, the gland be allowed to lie twenty-four hours before extraction. Hekma is of the opinion that this is a case of bacterial action, since with antiseptic fluids no formation of trypsin could be observed.

According to Schiff and Herzen, the spleen may have much to do with the formation of trypsin, since addition of splenic infusion or of splenic venous blood activates the pancreatic extract. This in Herzen's opinion is due to an internal secretion of the spleen.

The cleavage of proteids by trypsin goes on in the same way as that produced by pepsin, saving only that the end products are formed in less time in tryptic than in peptic digestion. However, hydrolytic cleavage of proteid may be carried further, if peptic digestion precedes the tryptic digestion (Gürber). Siegfried finds two peptones ($C_{10}H_{17}N_3O_5$, $C_{11}H_{19}N_3O_5$, molecular weights, 259 and 273 respectively), and Fischer and Abderhalden find a more complex residue containing all the monamino acids, which stubbornly resist further cleavage with trypsin.

Trypsin also dissolves gelatin, elastic substance and structureless membranes; likewise the gelatin-forming tissues, if they first be treated with acids or warmed to 90° C. Bokai states that trypsin does not act upon the nucleins; but after autodigestion of the pancreas, Kutscher found xanthin, hypoxanthin, and guanin —just the cleavage products of nucleic acids. Blood serum and serum globulin are not attacked by trypsin, although both are digested without difficulty by gastric juice.

The pancreatic juice of many mammals (human pancreatic juice uncertain) also coagulates milk, and according to Vernon the action is due to a special enzyme. Instead of paracasein, however, the clot contains a substance known as *metacasein*, which may represent a product of tryptic digestion of casein (Roberts).

C. LIPOLYTIC ENZYME, STEAPSIN

In 1846 Cl. Bernard observed that in the dog fat suffered digestive changes immediately after its entrance into the duodenum, whereas in the rabbit it took place somewhat farther from the pylorus. The cause of this difference he found to be the fact that in the dog the chief pancreatic duct opens into the intestine in common with the ductus choledochus quite close to the pylorus, while in the rabbit it opens some 30–35 cm. farther down. It follows that the pancreatic secretion must have a determining influence upon the digestion of fat. Further researches have shown that this effect consists in a cleavage of the fat into glycerin and free fatty acid. We shall discuss the importance of this cleavage more fully in our study of digestion in the intestine.

§ 5. BILE

Human bile as it flows from the liver is a beautiful reddish-yellow or yellowish-brown, or green, alkaline fluid, which on standing for some time in contact with the air assumes a green or greenish-yellow color. It contains a not insignificant amount of mucin, and the quantity of solids amounts to 1.5–4 per cent or more, of which 0.7–0.8 per cent is mineral.

The daily output of bile, taken from men with biliary fistulas, has been found to vary from 500 to 1,100 c.c.

During the intervals of digestion the bile does not flow into the intestine, but collects in the gall bladder, where by absorption of its water and mixture with bladder mucus, it becomes more concentrated, so that its content in solids may rise sixteen or seventeen per cent higher. The specific gravity of bile is 1.01–1.04.

The most important constituents are mucin, the bile acids, and bile pigments. The bile acids never occur free, but always as salts of the alkalies. They are compounds of glycocoll and taurin (amino-ethyl-sulphonic acid: $NH_2.C_2H_4.SO_2OH$) with cholic acid. Glycocholic acid ($C_{26}H_{43}NO_6$) and taurocholic acid ($C_{26}H_{45}NSO_7$) occur in different biles in relatively different quantities. In man the former is always present in greater quantity. Besides the usual cholic acid, whose formula is $C_{20}H_{31}\left\{\begin{matrix}CHOH\\(CH_2OH)_2\\CHOH\end{matrix}\right.$, two other acids, choleïc acid ($C_{24}H_{40}O_4$), and fellic acid ($C_{23}H_{40}O_4$) have been demonstrated in human bile. Numerous derivatives can be obtained from the bile acids.

The ***bile pigments*** are very numerous and they can be changed by various means into still others. Under physiological conditions we have, properly speaking, only two such pigments—the reddish-yellow, ***bilirubin***, and the green, ***biliverdin***. The former, which is easily crystallized in rhombic tablets, is to be regarded as the mother-substance of biliverdin and all other bile pigments.

Bilirubin has the formula $C_{16}H_{18}N_2O_3$ (Maly). It is transformed by oxidation into biliverdin $C_{16}H_{18}N_2O_4$, and *vice versa* the latter can pass by reduction into bilirubin again. *Biliprasin*, according to Dastre and Floresco, is to be regarded as an intermediate stage between the two. Bilirubin, acted upon by nascent hydrogen, is reduced to *hydrobilirubin* $C_{32}H_{40}N_4O_7$ which also occurs at times in the human bile. Since bilirubin and biliverdin are commonly present together in the bile, the color of the fluid is somewhere between red and green, and varies toward one or the other according as one pigment or the other predominates.

The bile contains also mucin, cholesterin, jecorin, lecithin, neutral fats and soaps, ethereal sulphuric acids, paired glycuronic acids, cholin, glycerin-phosphoric acid (both the latter, decomposition products of lecithin), and various mineral constituents, namely: the alkalies in combination with the bile acids, sodium chloride, potassium chloride, calcium and magnesium phosphate and iron. Sulphates occur, if at all, in very small quantities. A diastatic and a fibrin-splitting ferment have been demonstrated in the bile of certain animals; but it is not quite certain that they are formed in the liver, for they might represent enzymes only reabsorbed into the bile.

The following summary of analytical results with regard to the quantitative composition of bile may be given:

	Bladder bile.	Liver bile.
Water	82.3 –89.8 per cent.	96.5 –98.8 per cent.
Solids	10.2 –17.7 “	1.2 – 3.5 “
Mucin and pigments	1.3 – 2.5 “	0.1 – 0.5 “
Alkaline salts of the bile acids	3.0 – 6.8 “	0.2 – 1.8 “
Taurocholate	0.9 – 1.9 “	0.05 – 0.3 “
Glycocholate	2.1 – 4.9 “	0.2 – 1.6 “
Fatty acids derived from soaps	1.6 – 0.8 “	0.02 – 0.14 “
Cholesterin	0.3 – 0.4 “	0.05 – 0.16 “
Lecithin	1.2 – 0.4 “	0.005– 0.13 “
Fat		0.01 – 0.10 “
Soluble salts	....	0.7 – 0.9 “
Insoluble salts	....	0.02 – 0.05 “

The chief importance of bile in digestion appears to be that, in virtue of its bile salts it has the power to dissolve the free fatty acids and to increase the solubility of soaps; but more on this under the subject of absorption from the intestine.

Proof that the bile pigments are formed for the most part in the liver is found in the fact that when this organ is extirpated from birds, or when all the blood vessels of the liver and the bile ducts are ligated, not a trace of bile pigments can be demonstrated anywhere in the animal.

The bile pigments are universally regarded as derivatives of hæmoglobin. The following facts among others speak for this view. A pigment called *hæmotoidin* found in old blood stains is closely related to *bilirubin* and probably is identical with it. *Hæmatinic* acid, $C_8H_9NO_4$, which is the first oxidation product of *hæmatin* when oxidation takes place at the lowest possible temperature, appears to be identical with *biliverdinic* acid, an oxidation product of bilirubin (Küster).—When dissolved hæmoglobin is injected into the blood, or when substances which liberate hæmoglobin from the corpuscles are taken into the body, the quantity of pigments excreted in the bile increases materially.

Since it has been shown in these and other researches that the secretion of bile pigments never runs parallel to that of the bile acids, it follows that these two chief constituents are not derivatives of the same substance.

§ 6. INTESTINAL JUICE

The intestinal juice of man is a thin, clear, alkaline fluid containing epithelial cells, Bacteria and fat crystals, which effervesces on addition of acids. Freed of solid bodies by means of the centrifuge, it contains from 0.2 to 0.5 per cent Na_2CO_3, 0.2–0.6 per cent Cl, and about 1.1 per cent dry residue. Its specific gravity is in the neighborhood of 1.007 (Hamburger and Hekma).

Intestinal juice acts but feebly on starch. It inverts cane sugar, splits maltose, and, in young animals at least, also milk sugar. According to Röhmann and Nagano, the action of secreted intestinal juice on cane sugar and malt sugar is much less than that of the intestinal mucosa: it might be therefore that the cleavage of these sugars takes place in the mucosa itself, or that mere contact with the surface of the mucous membrane is sufficient for this purpose.

Emulsified fats appear to be attacked to some extent by the intestinal juice.

The native proteids, with the exception of casein and fibrin, are not digested by the intestinal juice. On the other hand, an extract of the intestinal mucosa in weakly alkaline or neutral reaction splits albumoses and peptones into simpler compounds: NH_3, leucin, tyrosin, lysin, arginin, histidin, etc. (Cohnheim). This action is heightened by warming the solution, and it is regarded therefore as the effect of a special enzyme called *erepsin.* The normal secretion (man, dog) has the same effect, only to a less extent, from which we may perhaps conclude that this cleavage of the primary products of digestion really takes place in the mucous membrane.

The nucleic acids are not decomposed by trypsin; but when they are exposed to the action of erepsin they are split into phosphoric acid and the purin bases. This fact speaks very strongly for the specific nature of erepsin (Nakayama).

Pawlow has discovered a new enzyme in the intestinal juice which he calls *enterokinase,* and which, as mentioned on page 252, transforms the raw mother-substance of trypsin in the pancreatic juice into the active enzyme. We know that this is not identical with erepsin from the fact that (in the human intestinal juice) the latter is destroyed by a temperature of 59° C., whereas the enterokinase is not destroyed below 67° C.

Gachet and Pachon, as well as Glaessner, assert that the glands of Brunner, which have an entirely different structure from that of the glands of Lieberkühn, secrete a proteolytic enzyme.

The glands of the large intestine produce no enzymes, but secrete a mucus which is of importance as a lubricant for the fecal mass.

SECOND SECTION

SECRETION OF THE DIGESTIVE FLUIDS

§ 1. GENERAL SURVEY

The secretory process presents many points of similarity in all digestive glands. For this reason, it is desirable to consider the process in broad outline before taking up in detail the peculiarities of the individual glands.

In the year 1851 Ludwig showed that section of the cerebral nerve supply to the salivary glands was followed by complete cessation of the flow of saliva (submaxillary, parotid). For hours there was not the least trace of fluid in the cannula which had been inserted into the duct. As soon however as the cerebral nerve was stimulated, saliva gushed out of the duct. In a thoroughgoing investigation, which is to be reported more fully under § 2, Ludwig demonstrated that this secretion is not a filtrate from the blood, but is produced by the specific activity of the gland cells under the influence of the nerves.

These discoveries stood quite alone for several decades. It is true that some observations were collecting, from which it appeared with a certain degree of probability that the secretion of the gastric glands and of the pancreas were influenced considerably by secretory nerves (Heidenhain, Richet *et al.*). But the existence of such nerves was conclusively proved by Pawlow only a few years ago. We do not know definitely even yet whether the other digestive glands, those of Lieberkühn, of Brunner, and the liver, are under the influence of secretory nerves in the same way as those already mentioned.

It would be a matter of the greatest interest to know exactly the anatomical connection between the secretory nerves and the gland cells. The many efforts of histologists in this direction have not been entirely successful as yet, although it has been stated recently that the nerves penetrate the membrana propria of the acini and terminate in end organs lying in direct contact with the secreting cells. The end organs are said to have either the form of mulberrylike clumps or of small twigs beset with nodules.

Under normal circumstances the secretion of those glands which are plainly under the control of the central nervous system is evoked by reflex action, set up in many cases by perfectly definite chemical substances (Pawlow) (cf. page 264). These reflexes as a rule stand in a very close relationship with the ingestion of food, and in general it may be said that in the intervals of digestion when there is no desire for food, the digestive fluids are secreted only in very small quantities.

Bile forms an exception to this rule, since even in the fasting condition it is produced and is given off by the liver. Possibly this is due to the fact that bile is not only a digestive fluid, but contains also various substances which, so far as our knowledge at present goes, have no significance whatever in digestion, and must be looked upon as real waste products. As such they would naturally be produced continuously, just as in the case of urea and the decomposition products found in the expired air. However, the bile passes into the digestive canal only after the ingestion of food; in the meantime it is being stored in the gall bladder.

In 1868 Heidenhain published the important observation that after long-continued activity the submaxillary gland exhibits morphological changes, and some years later he ascertained that the same is true of the parotid and of the fundus glands of the stomach. Investigation in this direction was extended by several other authors, and it has been proved by their work that while the gland is resting—i. e., is not pouring out secretions—a substance is being laid down within it in the form of small granules, which to a greater or less extent disappears during the activity of the gland. This substance must be regarded as the source of the specific constituents of the glandular secretions.

Heat is generated by the glands in the act of secretion. Cl. Bernard (1856) found the temperature of the hepatic blood constantly higher than that of the portal blood. At the time of active secretion of bile the difference rose to 0.7°–0.9° C. The following year Ludwig and Spiess observed that the temperature of the submaxillary saliva may be more than 1° C. higher than that of the blood in the carotid of the same side. The increase in oxygen consumption and of carbon-dioxide production indicate a highly active metabolism going on in a working gland; both are three to four times as great in a strongly active condition of the submaxillary as in a resting condition (Barcroft).

Attention has already been directed to the electric phenomena of glands (page 48). Bayliss and Bradford report that on stimulation of the cerebral secretory nerves of the dog, a strong electric variation is produced both in the submaxillary and in the parotid, since the surface of the gland becomes negative to the hilus. Stimulation of the sympathetic produced an opposite variation—the surface becoming positive to the hilus. Moreover, they showed that these electrical variations are not due either to alterations of the blood flow or to the flow of the secretion through the duct. On the basis of these and other observations, the authors conclude that the negativity of the surface toward the hilus is the result of a passage of fluid through the wall of the acini or is the result of changes in the gland cells set up by stimulation, which precede the passage of the fluid. The positivity of the surface would be the expression of those changes in the gland cells by which the organic constituents of the secretion are formed.

§ 2. THE SALIVARY GLANDS

A. SECRETORY NERVES

The salivary glands receive their nerves by two different pathways, namely the cerebral and the sympathetic. The former were demonstrated by Ludwig as mentioned on page 256; while the discovery that the sympathetic can cause secretion of saliva we owe to Eckhard.

In the dog the cerebral nerves to the submaxillary and sublingual glands proceed from the facial nerve through the chorda tympani to the lingual branch of the trigeminal, and from this along the ducts to the gland. The cerebral supply to the parotid of the dog springs from the glossopharyngeal and reaches the auriculo-temporal branch of the fifth nerve through the nerve of Jacobson, the small superficial petrosal, and the otic ganglion.

The sympathetic fibers run in the cervical sympathetic trunk to the superior cervical ganglion, and from there follow the blood vessels to the hilus of the appropriate gland.

Ganglion cells are interpolated in the course of these nerves—those of the sympathetic fibers for the sublingual and submaxillary being located in the superior cervical ganglion. The ganglion cells of the cerebral secretory fibers for the sublingual gland are distributed as small ganglia over the entire gland (to these belong also the sublingual ganglion); those for the submaxillary lie for the most part in the hilus of the gland itself (Langley).

On stimulation the different secretory nerves give different results, which vary with the species of animal experimented upon. We shall consider here only the results obtained in the dog.

Stimulation of the cerebral fibers to any of the glands causes almost immediately a copious secretion of a fluid poor in solids, which may continue for hours, if the stimulation be maintained at the proper strength. The secretion produced from the submaxillary by excitation of the sympathetic appears later. At first a few drops of a fluid rich in solids come from the duct, then the secretion ceases, but reappears on continued stimulation. The parotid as a rule gives no secretion on stimulation of the sympathetic, probably because the thick fluid stops up the duct.

Since stimulation of the cerebral fibers causes a considerable dilatation of the blood vessels of the gland and a consequent increase of blood flow (as much as six times the original) (cf. page 234), whereas stimulation of the sympathetic causes vasocontraction and a considerable decrease of blood flow, it might be thought that the difference in the secretion in the two cases is due to the difference in the amount of blood supplied. But this is not true. For if the arteries of the gland be entirely closed off and the cerebral fibers be then stimulated, the quantity of secretion obtained is smaller, but it has all the properties of the normal cerebral saliva and its percentage content of solids is not greater than when the circulation is unhindered.

Heidenhain, with some reservation it is true, has sought to explain these phenomena as follows. He supposes that every gland is provided with two kinds of nerve fibers: (1) those which preside over the transudation of water and of the salts, the "secretory fibers," and (2) those which control the formation of the soluble constituents and the growth of the protoplasm, the "trophic fibers." These fibers occur in the different nerves of the glands in different numbers. Thus the cerebral fibers in the dog would be relatively poor in trophic but relatively rich in secretory fibers, while the sympathetic would contain only a few secretory but many trophic fibers.

It is not to be denied that Heidenhain has brought many facts to the support of this view. For example, simultaneous stimulation of the sympathetic and the glossopharyngeal in the dog increases considerably the percentage composition of solids in the parotid saliva. But it is not possible to explain all the known facts concerning the influence of nerves on the salivary secretion from this point of view. Thus if the glands be poisoned, not too severely, with atropine, stimulation of the chorda is entirely without effect at a time when stimulation of the sympathetic is still effective. Now it is very probable that atropine acts so as to paralyze the end organs of the cerebral fibers, and from the fact just given we know that this poison acts upon the end organs of the two nerves in an entirely different way. Hence we can scarcely say that the sympathetic and the chorda are composed of the same kinds of fibers in relatively different numbers (Langley).

The discovery of Gerhardt with regard to *morphological changes* in the submaxillary after section of the sympathetic and of the chorda, speaks to the same effect. In the former case the protoplasm remains unchanged, whereas the nucleus shrinks, although not in all cells; after section of the chorda the nucleus remains normal, but the protoplasm in many cells undergoes significant changes, becoming turbid, finely granular and opaque.

A further difficulty for Heidenhain's theory is the so-called *paralytic secretion* discovered by Cl. Bernard. Some twenty-four hours after section of the cerebral nerves, the submaxillary gland begins to secrete, slowly at first, then faster and faster until within a week a drop issues from the duct every twenty minutes. It makes no difference whether the sympathetic is injured or not; section of this nerve produces no paralytic secretion. In the course of time after section of either nerve the size of the gland gradually diminishes, and the gland acquires a waxlike appearance.

A priori it might be supposed that secretion is only a *process of filtration* from the blood through the capillary walls. But we have great difficulty on such an hypothesis to account for the chemical properties of the secretion; for several substances found in the secretion and in the glands are not found at all in the blood, and must, therefore, be formed in the gland cells. This is attested also by facts to be discussed later with regard to morphological changes appearing in the glands. But more convincing is the following. If the duct of the submaxillary gland be connected with a Hg-manometer and the cerebral nerve be then stimulated, the mercury in a very short time, even within twenty-five seconds, rises 100 mm. higher than the mercury in a manometer connected with the carotid. That is, the secretion pressure becomes higher than the blood pressure. Finally, the remotest possibility of regarding the secretion as a process of filtration is excluded by the fact that stimulation of a secretory nerve causes a flow of saliva in animals which have been bled to death.

When a nerve is stimulated, the constituents already deposited in the gland cells during rest are not only given off, but there is at the same time an *increased production* of them. This is plainly indicated by the fact that the quantity of nitrogen in both the secreting gland and its secreted saliva is greater than that of the resting gland on the other side (Pawlow). When the nerves are excited with stimuli of increasing strength, not only does the absolute quantity of the secretion and of its solid constituents increase, but the percentage content of the latter rises higher the more rapid the rate of secretion becomes. This increase always affects the inorganic constituents, but not the organic, unless care be taken not to fatigue the gland by overwork. If the gland be fatigued, the percentage content of organic substances may even decline in the face of an increased rate of secretion.

We may summarize the effects produced in the glands by stimulation of their nerves as follows: (1) A change takes place in the gland cells developing certain forces which are expressed by the act of secretion; (2) at the same time an increased formation of the specific constituents of the secretion appears; and (3) if the stimulation continue for a long time, the gland gradually becomes fatigued, so that the delivery of secretory products exceeds the new formation of specific constituents.

Under normal circumstances the secretion of saliva is caused by a *reflex act* induced chiefly from the mouth, and Pawlow has shown that the quantity as well as the quality of saliva in the dog is adapted with extraordinary nicety to the properties of the substances introduced into the mouth.

Mechanical stimulation of the buccal mucous membrane does not always produce a flow of saliva. If, for example, a handful of pebbles be thrown into a dog's mouth, the dog moves them to and fro in his efforts to get rid of them, but no saliva, or at most only a drop or two, is poured out. If on the other hand sand be used instead of pebbles, a copious flow of saliva is set up, because the sand cannot be removed from the mouth without a stream of fluid. Nor is there any discharge of saliva from application of water or snow, but with acid, salty, bitter or caustic substances which require to be diluted or washed out of the mouth, a discharge at once occurs.

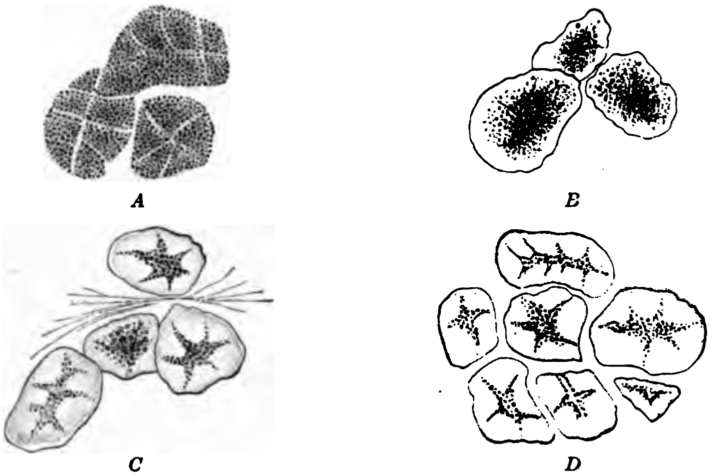

Fig. 100.—Parotid gland of the rabbit as seen in a fresh, unstained preparation, after Langley. *A*, resting state. *B*, after injection of a slight quantity of pilocarpine. *C*, after stimulation of the cervical sympathetic. *D*, the same, only a stronger effect.

In all these cases the saliva is thin, watery and contains only a trace of mucin. But with all kinds of edible substances a viscid, mucous saliva is secreted such as is necessary to facilitate swallowing the bolus. Besides, the quantity of saliva depends upon the dryness of the food: the drier it is, the more saliva.

It is unnecessary actually to place the stimulant into the mouth in order to produce a flow of saliva. *Sight or smell* of it is sufficient, or indeed, as our own experiences prove, *imagination* even of savory substances will produce the effect. With regard to the quality and quantity of saliva, the same differences are observed as when the stimulus is applied to the mouth cavity: from which we may conclude that a psychical influence of no small value is involved, although this cannot be exercised by direct effort of the will.

The *salivary nerve centers* are located in the medulla; for reflex secretion is obtained after transsection of the brain in the pons. A puncture in the medulla is followed likewise by secretion. Unilateral injury to the floor of the fourth ventricle a little behind the origin of the trigeminal nerve causes secretion in both submaxillary glands and in the parotid of the same side. Both cerebral and sympathetic nerves are roused to activity in this case. It is possible that the glands on each side of the body have their own centers, and that these are connected together by commissures (Beck).

The salivary glands can be set in action also by artificial stimulation of that part of the cerebral cortex which corresponds roughly to the motor zone. It is very probable that the above-mentioned psychical influence on the salivary glands depends upon this cortical field.

B. MORPHOLOGICAL CHANGES DURING SECRETION

The more recent investigations of this subject have been made upon practically *fresh material* instead of, as formerly, upon preserved material. We shall follow the descriptions given by Langley and by Biedermann.

In the *albuminous glands* (Fig. 100) Langley found that in the resting state, the cells are filled with a *collection of granules* so abundant as to obscure the cell boundaries. When the gland has secreted for some time, the cells increase in size, the granules gradually disappear especially from the outer zone, or the side toward the membrana propria, while the inner zone or the side toward the lumen of the gland still contains granules. These changes are constant whether the gland be caused to secrete by the natural stimulus, by injection of pilocarpine, or by stimulation of its nerves.

According to E. Müller, there occurs here a conversion of strongly refractive granules into feebly refractive ones, which pass into the secretion as small spherical drops—the so-called secretion vacuoles (Fig. 101; cf. also Fig. 99). In very active secretion the first-named granules pass directly over into the secretion vacuoles. When they leave the gland cells they pass first into the secretory capillaries running between the cells where they are dissolved and whence the secretion flows into the ducts of the gland.

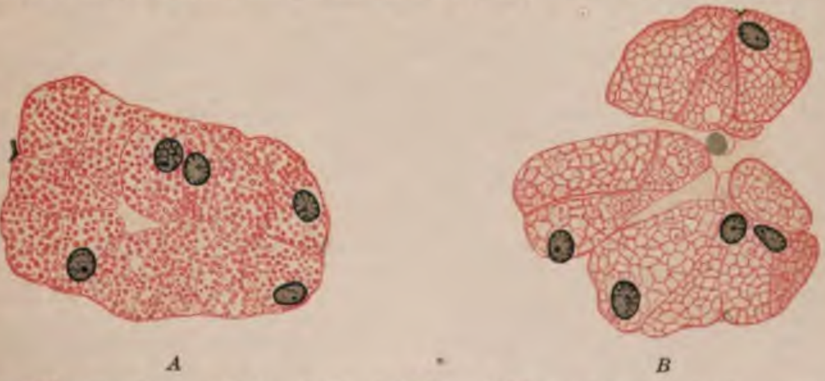

FIG. 101.—Parotid gland of the cat, after E. Miller. Sublimate fixation. *A*, after twenty-four hours' fast. *B*, during active discharge of the secretion.

We meet with similar phenomena in fresh preparations of the *mucous glands*. A gland from the tongue of *Rana esculenta* teased in a 0.6-per-cent salt solution (Biedermann) almost always shows cells, which in the ends turned toward the lumen are thickly set with dark, strongly refractive granules. When the same object is observed in active secretion the dark granules have disappeared for the most part, or form only a narrow border along the inner edge of the cells. The latter contain also clear, vacuolar drops (Fig. 102).

From these observations it appears that in the albuminous as well as in the mucous glands, a substance is formed during the resting state, which in the fresh gland has the form of small granules. This substance is liberated from the cells in the act of secretion and as a consequence the cells decrease in size, especially after a copious discharge; the main part of the cell is now clear.

Are the specific constituents of the secretion derivatives of the living protoplasm, or are they to be regarded as products of its activity? This question cannot be answered definitely at present. Heidenhain conceived that in the mucous glands at least the cells as a whole are converted into the secretion, and that the so-called demilume cells of Gianuzzi are young cells destined to replace the mucous cells after their disintegration. This assumption however is not in accord with the fact that cell divisions are very rarely met with in secreting glands. That cells do occasionally perish in very active secretion and can be replaced by division, has nothing whatever to do with the process of secretion as such. And as for the demilumes, they appear from recent researches (Stöhr, Noll) to be simply empty mucous cells.

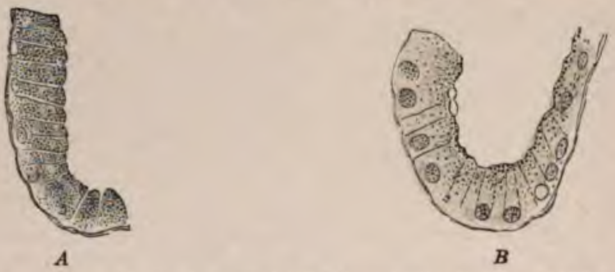

FIG. 102.—Parts of a tongue gland of the frog (*Rana esculenta*), fresh condition, after Biedermann. *A*, resting state. *B*, after stimulating the glossopharyngeal nerve for three hours.

Other investigators, with Altmann at their head, regard the granules as morphological derivatives of formed constituent elements, and claim that the manner of their origin, their growth and their transformation indicate that they are vital units.

From all that we know, however, the granules found in the resting gland might just as well represent products of the metabolic activity of the protoplasm; hence no destruction of living substance would be involved in their formation. The material at hand is by no means sufficient to decide a question fundamentally so important.

§ 3. THE GLANDS OF THE STOMACH

A. SECRETORY NERVES

Early observations on the secretion of gastric juice for the most part tended to show that this process scarcely came within the control of the central nervous system. Some few observations there were, it is true, which indicated such an influence, but they were rather scattered and were outnumbered by other observations which made it more likely that the extrinsic nerves to the stomach had no influence of a direct kind upon its secretory activity. In the year 1889, however, Pawlow and Schumow-Simanowsky demonstrated that the vagus contains secretory fibers for the gastric glands.

Richet had found in the case of a man with an œsophageal stricture and upon whom a stomach fistula had been made, that chewing strongly sapid foods produced immediately a flow of gastric juice from the fistula. It was natural to regard this secretion as a reflex.

The above-named authors undertook to establish this conclusion experimentally, and for the purpose made on dogs an œsophageal fistula besides the usual stomach fistula. When the animal received something to eat and swallowed a bolus, it of course came out through the opening in the neck without ever reaching the stomach ("fictitious feeding"). Nevertheless, after a latent period of five to six minutes a copious secretion of gastric juice made its appearance. In this way it was proved that the secretion can in fact be called out reflexly.

The *efferent nerves* concerned in this reflex are the vagi. If the vagi be cut, the reflex fails. If they be stimulated a clear fluid begins to trickle from the fistula, which in comparison with the normal gastric juice shows a lower acidity, but digests proteids. In addition to these the vagus appears to contain also fibers which inhibit the glands of the stomach.

But the secretion of gastric juice is not dependent alone upon the vagus. There are perfectly trustworthy statements in the literature which show that the secretion does not cease after section of the vagi, although the reflex from the mouth be excluded; but that animals thus operated upon digest their food in the stomach. Besides, analysis of the urine reveals no products of abnormal putrefaction in the alimentary canal of such animals, and we may conclude that a real gastric juice is secreted which contains just as much hydrochloric acid, but considerably less pepsin, than the normal juice.

Thus there are two modes of gastric secretion, namely, one under the influence of the secretory nerve fibers which traverse the vagus, and the other independent of those fibers.

(1) *The Secretion under the Influence of the Vagus.*—Neither excitation of the nerves of taste, nor the act of chewing, nor the movements of deglutition have of themselves any power to cause a reflex secretion of gastric juice. Only when the animal exhibits some desire for food does secretion result. The imagination of savory substances would seem therefore to be of special importance, and this is confirmed by the fact that gastric secretion occurs when one merely offers a dog a piece of meat without giving it to him. This "*psychical*" *secretion* is at times very abundant; but if not, the amount of secretion is considerably increased by fictitious feeding. From these and similar facts it appears that although excitation of the afferent nerves from the mouth and the œsopha-

gus does not of itself produce any gastric secretion, yet when the animal has some desire for food this excitation intensifies considerably the psychical secretion which would otherwise take place, and raises both the acidity and the digestive power of the secretion.

In the case of a five-year-old boy with a complete œsophageal stricture and a gastric fistula, Hornborg found that chewing palatable foods induced, after an average latent period of seven minutes, a secretion which lasted for forty minutes or more, whereas chewing disagreeable foods, or chemically active (lemons) or indifferent substances (rubber) was without any influence on the gastric glands. It is worthy of note that the secretion failed when the boy was not permitted to eat immediately food particularly palatable to him, and began to cry; also that every time he was fed through the stomach fistula he wished for something edible to chew. Mere sight of food was not effective in provoking the secretion.

(2) *The Secretion Independent of the Vagus.*—*Mechanical stimulation* of the stomach mucosa, even when it is very energetic, causes no secretion of gastric juice whatever; only an alkaline mucus flows from the fistula (Pawlow). The secretion not mediated by the vagus must be the result, therefore, of *chemical stimulation.* In order to study this question more closely and to prevent mixture with foreign substances, Heidenhain separated the fundus portion from the rest of the stomach by a surgical operation, and thus prepared an isolated "fundus fistula." In this operation the branches of the vagus which mediate the secretory reflex were cut. Nevertheless, when the animal received something to eat secretion appeared in the blind sac. It began fifteen to thirty minutes after eating and continued for a longer or shorter time according to the quality and quantity of the food—after a moderately full meal, thirteen to fourteen hours; after a very full one, sixteen to twenty hours. When the dog was given very slightly digestible food, such as coarsely chopped ligamentum nuchæ, no secretion appeared, but began when he was subsequently allowed to drink. Even then the secretion continued for only a short time, one and one-half to four hours at most.

Pawlow and Chigin carried out even more detailed experiments on dogs in which the blind sac was prepared without section of the vagus branches. The substances whose effects on the mucous membrane were to be tested were introduced (without the dog's knowledge) through a fistula directly into the main part of the stomach. Water, 0.1–0.5-per-cent HCl solutions, etc., in quantities of 100–150 c.c. exerted only a very slight influence on the process of secretion in the isolated sac. In quantities of 500 c.c. pure water, ten-per-cent solutions of cane sugar or starch, or egg albumin provoked a somewhat stronger secretion. This began in a majority of cases after thirteen to twenty-nine minutes. Since distilled water evoked just as much secretion as the solutions, it is assumed that the effects here are only those of the solvent. Weak soda solutions reduced the effect of water. Fats also exerted an inhibitory influence.

When *meat gravy, meat juice* and *meat extract* or *milk*, or a solution of gelatin in water were introduced into the stomach in the same way, results were very different. An abundant secretion began after an average latent period of thirteen minutes, which continued for about three hours. Neither egg albumin nor albumose nor bread had any such effect. It appears therefore that certain extractives contained in meat, to which however creatin and creatinin do not belong, certain constituents of milk, etc., are specific stimuli for the stomach. Furthermore, there are experiments which show that once the secretion is started by these substances, it is considerably augmented when, for example, egg albumin, of itself but slightly active, is introduced. In the same way starch introduced with meat can intensify the secretory process considerably.

From these observations we can form provisionally the following conception of the *conditions for secretion in the stomach*. Secretion of gastric juice is started by a complicated reflex process, which is set in operation by the sight of food as well as by its passage through the mouth and œsophagus, and is mediated by the vagus. This secretion itself lasts for a fairly long time; but it is augmented by the stimulating influence on the mucous membrane of ingested water and, above all, of certain extractives, etc., contained in the food.

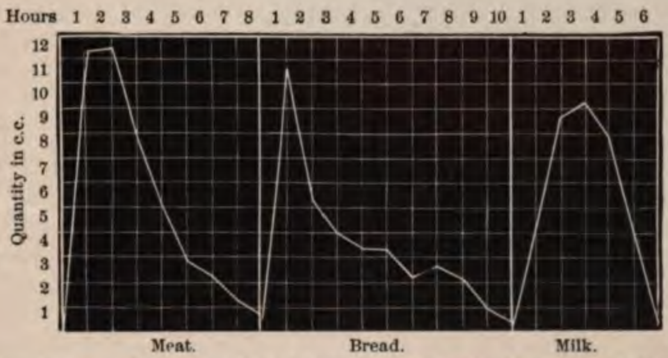

FIG. 103.—Hourly course of secretion of gastric juice in the dog's stomach, after Pawlow. Exclusive diets of meat, bread, and milk were given.

Chigin's experiments on the course of the secretion in the blind sac with the vagi preserved show very instructively how the activity of the mucous membrane under the influence of the vagus reflexes and the excitation of the food, is adapted to the momentary requirements upon it. With all the articles of food thus far tested the secretion began at about the same time. It reached its maximum during the first or the second hour (with milk during the third hour). After the maximum was reached the secretion fell immediately and became gradually less and less until it finally ceased. The absolute quantity of gastric juice with the same article of food was greater, the greater the mass of food introduced. The quantity secreted, for example, was greater with 200 g. of meat than with 200 g. of bread or 600 g. of milk (Fig. 103). The digestive power of the fluid secreted with the articles of food just mentioned, when tested from hour to hour, shows characteristic variations (Fig. 104). Feeding meat,

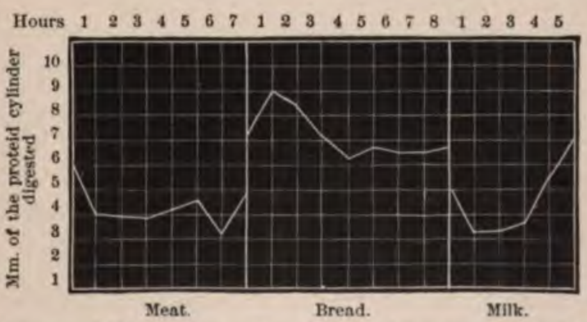

FIG. 104.—Hourly course of the digestive action of gastric juice on proteid, after feeding exclusively meat, bread, and milk (Pawlow).

milk and bread with the same N-content (about 3.4 g.), there appeared in the isolated sac 27, 34 and 42 c.c. respectively of gastric juice having a digestive power of 4.0, 3.1 and 6.16 mm. of egg albumin (cf. page 245). Since the digestive power is proportional to the square root of the quantities of pepsin, the quantities in this series would be to each other as 430, 340, and 1,600.

The center of these reflexes mediated by the vagus probably coincides with the vagus nucleus. The psychic influence on the secretion is exercised naturally through the cerebrum. In the dog Bechterew obtained a secretion of gastric juice and of gastric mucus on stimulating a region lateral to the anterior portion of the gyrus sigmoides just at the forward end of the third convolution. Stimulating for four to five minutes the secretion continued for thirty to fifty minutes and exhibited an unmistakable similarity with that obtained by fictitious feeding. After extirpation of this cortical field no secretion appeared on offering food.

The mechanism of the secretion which is independent of the vagus is much more difficult to explain. It might be caused either by some reflex process or by the direct exciting effects of absorbed substances upon the glands themselves. There are difficulties in the way of both hypotheses and the matter cannot be regarded as settled.

B. THE GASTRIC GLANDS

The *mucous membrane of the stomach* presents considerable differences between the fundic and pyloric portions. The pyloric portion is pale and whitish in color and is beset by a few high folds, here and there united together. The rest of the mucous membrane has a reddish-yellow or reddish-gray color, and possesses numerous folds bound together into an irregular network, and in addition to these, fine secondary folds likewise arranged as a net. Into the depressions formed by the folds open the gastric glands, whose epithelial cells are continuous with the epithelium which clothes the free surface of the membrane.

This superficial epithelium secretes the gastric mucus and behaves probably like similar cells of the salivary glands.

The glands of the mucous membrane are tubular and belong to *two different types,* one constructed of one kind of cells, the other of two kinds. The spatial distribution of the two kinds presents certain differences in different mammals. In the dog and man the glands formed of one kind of cells occur only in the pylorus; those with two kinds occur only in the fundus. For this reason they are named pyloric and fundic glands respectively. The boundary between the two divisions of the mucous membrane is not however very sharp.

The secreting elements of the pyloric glands are cylindrical cells arranged in a single layer upon the basement membrane of the glands. The fundic glands contain similar cylindrical cells similarly arranged. These cells were discovered by Rollet and Heidenhain, and are called the *chief* or *adelomorphous* cells.

In addition to the chief cells and situated outside of them are other so-called *parietal* or *delomorphous* cells. These lie between the chief cells and the membrana propria, but do not form a continuous layer. Just as in the salivary glands, there are fine secretory capillaries between the gland cells. Those belonging to the parietal cells surround them in a basketlike fashion and are connected by cross ducts with the lumen of the gland (Fig. 105).

It has been known for a long time that the pepsin is formed in the chief cells (Wassman, 1839).

If small pieces of the fundus mucosa be digested in a warm place with dilute hydrochloric acid, they dissolve leaving only small flakes behind. Boiled white of egg digested at 35°–40° C. in acidulated water, to which a small piece of the fundic mucosa has been added, dissolves in one to one and one-half hours.

Since it had been observed further that the pylorus mucosa withstood digestion much longer on similar treatment, and since the chief cells had not yet been discovered, it was supposed that the fundic glands were the only seat of pepsin production, and that the pyloric glands produced only mucus like the superficial epithelium. It has since been proved that the pyloric glands also produce pepsin.

Simply to make an extract of pylorus mucosa and demonstrate pepsin therein, would not be a fair test, for it might be that the pepsin came from the gastric juice and had only been absorbed by the pyloric mucosa. The matter takes quite another aspect however when we discover that the pyloric mucosa is not completely freed of its pepsin by washing for forty-eight hours in running water. Several other observations show the same thing, and conclusive evidence is furnished by the following: By an operation the pyloric portion can be isolated from the rest of the stomach in the same way as has already been described for the fundic portion, and a pyloric fistula be thus established (Klemensiewicz, Heidenhain, Akerman). The animals recover and exhibit no sort of disturbance in their general health. From this pyloric sac a fluid is obtained which always contains pepsin even if collected weeks or months after the operation. There can be no question here of absorption from the gastric juice.

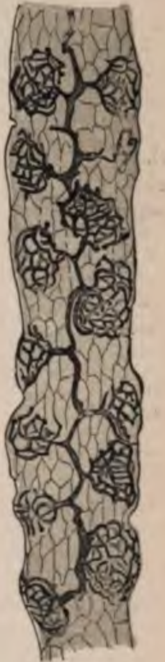

FIG. 105.—Secretion capillaries surrounding the parietal cells of the gastric glands in a basketlike network. The capillaries also penetrate the cells, after E. Müller.

We have still to decide, however, whether the pepsin is formed in the chief or the parietal cells of the fundic glands. Several facts indicate the former.

(1) If freshly isolated fundic glands be warmed in a drop of dilute hydrochloric acid under the microscope, the chief cells may be seen to disintegrate rapidly, whereas the parietal cells only swell up and become transparent. (2) In sheep embryos it has been observed that the parietal cells appear first in the course of development and the chief cells much later. Pepsin produc-

tion can be demonstrated in the mucous membrane only after the latter appear. (3) If different parts of the stomach mucosa be extracted, it is found that the quantity of pepsin shows no dependence upon the number of parietal cells in the different parts, but varies in direct proportion to the number of chief cells.

How far the parietal cells participate in the formation of pepsin must be regarded as still an open question. In various lower vertebrates whose gastric glands possess cells of only one kind, it has been observed that both pepsin and hydrochloric acid are produced. But we cannot draw any positive conclusion with respect to the more differentiated gland of the higher vertebrates from this discovery.

Weight for weight the pyloric mucosa produces much less pepsin than does that of the fundus—which is quite intelligible when we consider that the fundic glands are much more thickly set than the pyloric glands, and also that the length of the former is considerably greater than that of the latter.

The amount of rennin of the gastric juice during the different stages of digestion always runs parallel to the amount of pepsin. From this and other facts it appears permissible to conclude that although rennin is not identical with pepsin (page 250), it is formed in the pyloric glands as well as in the chief cells of the fundus glands. Whether it originates in the parietal cells also cannot yet be decided.

Views are widely divergent as to the seat of hydrochloric acid production. While some assume that it is produced in all the gland cells of the stomach, others suppose that it originates only in the parietal cells of the fundic glands.

As a matter of fact it appears to be shown with a fair degree of certainty that the pyloric glands do not produce hydrochloric acid, for in the secretion of the isolated pyloric sac one finds in exceptional cases an alkaline reaction and, what is important also, the mucous membrane of the blind sac exhibits at such times perfectly normal properties throughout. Moreover, it is stated that the free surface of the mucosa gives an acid reaction only in places where glands with two kinds of cells are found; at other places it reacts alkaline.

After considering all the facts obtainable bearing on this subject, Heidenhain came to the conclusion that hydrochloric acid is formed in the parietal cells of the fundic glands. It must be stated, however, that he reached this conclusion by the process of exclusion and not by direct evidence.

The cells of the gastric glands in the process of secretion undergo *morphological changes* which have been followed by Langley on fresh preparations. In the fasting condition the chief cells are strongly granular, but during digestion are clear—i. e., the outer zone (about one-third to one-half of the entire cell) shows no granules; they occur only along the luminal border of the cell. Extracts from different parts of the mucosa yield pepsin in greater abundance, the richer the glands in granules.

We find therefore the same state of affairs in the cells of the gastric glands as in the salivary glands. During the fasting period a substance is laid down in the chief cells, which in fresh preparations appears in the form of granules. During the act of secretion this substance is gradually used up; at the same time a new formation of the substance is going on, as we know from the fact that the percentage of pepsin of the mucosa increases again after the ninth hour of digestion.

C. WHY DOES THE STOMACH NOT DIGEST ITSELF?

Several hypotheses have been put forward to account for the fact that the stomach does not digest itself. The mucus of the stomach might act as a kind of varnish to protect the mucosa itself from the action of the gastric juice, or the epithelium of the mucosa might preserve the underlying parts in some way, or the gastric juice might be neutralized by the alkalinity of the blood, or the mucosa might be absolved from the destructive action of the gastric juice by its absorption. However, many objections can be urged against all of these hypotheses as well as the experimental facts underlying them, and the question was left to a certain extent undecided by simply assuming that the proteolytic enzymes cannot act upon the living cells of the same body.

A nearer approach to an explanation seems to have been attained in Weinland's discovery of an antipeptic and antitryptic action of the stomach and intestinal mucosa. This action is probably due to antienzymes which are found throughout the whole animal scale, and occur not only in the intestinal tract but also in cells of other organs. As mentioned at page 155, such antienzymes are present also in the blood.

§ 4. SECRETION OF PANCREATIC JUICE

A. SECRETORY NERVES

That the secretion of pancreatic juice is to a certain extent under the control of the central nervous system was rendered very probable by the fact, ascertained by Heidenhain, that it can be started up or accelerated by electrical stimulation of the medulla oblongata. Later Pawlow succeeded in completing the evidence of secretory nerves to the pancreas.

These nerve fibers traverse the vagus. If, with the observance of certain precautions which are necessary to shut out the restraining influence of various sensory stimuli, the vagus be stimulated, a more or less active secretion of pancreatic juice is plainly demonstrable. The vagus also conveys *fibers which inhibit* the pancreatic secretion.

The *splanchnic* likewise contains secretory fibers for the pancreas, but its action is much less powerful than that of the vagus (Kudrewetsky).

Secretion of the pancreatic juice in the herbivorous animals is continuous —a condition doubtless connected with the continuous character of digestion in these animals. In the carnivora it is intermittent, and (in the dog) the first drops flow from the duct one and one-half to three and one-half minutes after eating. In man also a rise occurs after eating and reaches its maximum in the fourth hour, from which time on it gradually falls (Glaessner; Fig. 106).

To what extent the secretion of pancreatic juice is caused like that of the gastric juice by stimuli from the mouth, or what rôle the psychic factor plays in the process must remain for the present undecided. However, still another influence is of far-reaching importance here. If an acid (no matter what one) be introduced into the duodenum, after a short latent period, a copious secretion of pancreatic juice is poured out. The acid gastric juice flowing through the pylorus obviously must have exactly the same effect (Gottlieb, Pawlow). As soon as the pyloric sphincter opens and gastric juice pours out into the small intestine, the conditions are present for an abundant flow of pancreatic juice.

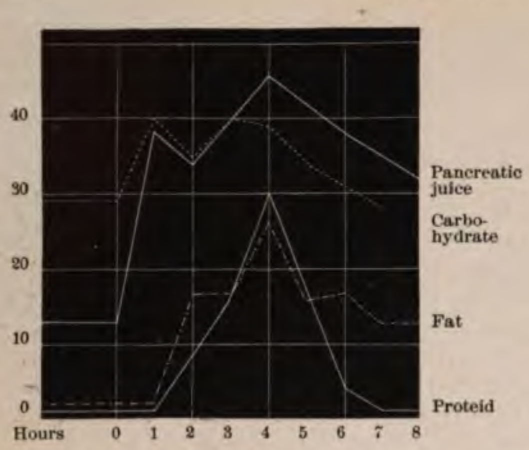

FIG. 106.—The course of pancreatic secretion in man, after a meal consisting of soup, meat, and rolls, after Glaessner.

This influence of acids is beautifully confirmed by the fact that a flow of pancreatic juice caused by the gastric secretion is reduced considerably when the stomach contents are neutralized by administration of alkaline fluids.

Since the vagus causes the flow of gastric juice also, it might be thought that the secretion of the pancreas under the influence of this nerve begins only under the stimulating action of the acid gastric juice. But this is not true, for on artificial stimulation of the vagus the pancreas begins to secrete *sooner than the stomach*, and besides, the pancreatic secretion makes its appearance even if the pylorus be firmly ligated so as to prevent any passage of gastric juice (Popielski).

Water and neutral fats in the intestine are mentioned by Pawlow as special excitants of the pancreatic secretion (in man administration of fat was without effect); other authors have succeeded in inducing a secretion by means of mustard, pepper, chloral hydrate, ether, etc.

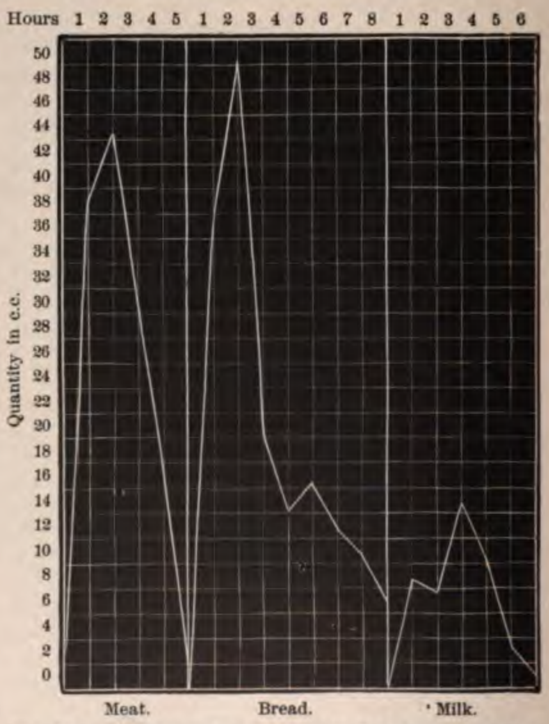

FIG. 107.—The course of secretion in the pancreas of the dog, after feeding exclusively with meat, with bread and with milk, after Walther.

Formerly it was supposed that this secretion is in the nature of a reflex and is mediated by the afferent nerves of the small intestine. It could be pointed out in support of this view that injection of acids into the rectum or directly into the blood evoked no secretion, and that therefore the glands could not be stimulated from the blood. Bayliss and Starling, however, observed that an extract of the intestinal mucous membrane with HCl, injected into a vein, called forth the pancreatic secretion at once. The acid dissolves out of the mucous membrane a substance, not destroyed by boiling and called by the authors *secretin*, which in their opinion acts specifically upon the pancreas and constitutes the only natural cause of its secretory activity.

Beyond all doubt *secretin* is a powerful excitant of the pancreatic secretion; but its specific nature is denied by several authors. Since, however, CO_2 from the small intestine also produces a flow of pancreatic juice, and there is of course no secretin extract of the mucosa in this; since, further, the acid introduced into an intestinal loop has an exciting action on the pancreas, even when the venous blood of this loop is diverted and the thoracic duct is tied off, one is justified in the assumption that on introduction of acid into the intestine the secretion is produced partly by a reflex set up by the acid, and partly through the secretin in the blood.

Nothing definite can be said concerning the nerve centers of pancreatic secretion. The observations which purported to demonstrate reflex centers in the gland itself are no longer convincing since the discovery of secretin.

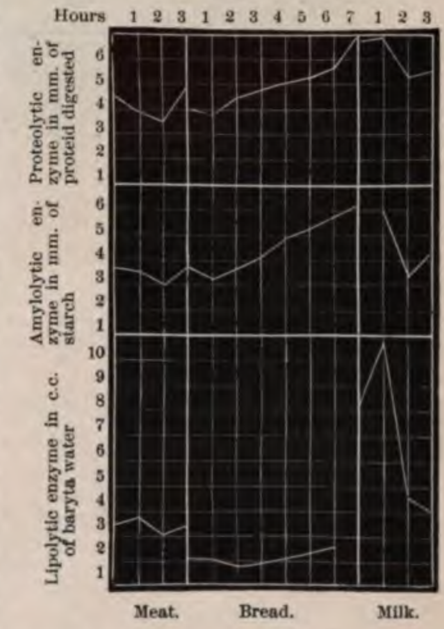

FIG. 108.—The enzymes of panceratic juice, after feeding exclusively with meat, with bread and with milk, after Walther.

The hourly course of the secretion, which appears to be connected with variations in the discharge of the stomach contents into the intestine, as well as the amount of the different enzymes present in the secretion, shapes itself according to the food ingested, as may best be seen from the diagrams in Figs. 107 and 108.[1]

From these diagrams it is evident that the absolute rate of secretion following milk is different from that following the ingestion of meat and bread; that the content of amylolytic enzyme is considerably greater for bread than for meat and milk, and that the content of steapsin is much greater for milk than for meat and bread.

The total quantity of nitrogen which is given off in the pancreatic juice during a period of digestion varies much with different foods. In fact with the same amount of N in the food, it is about twice as great for bread as for milk or meat, and in the former case rises to about one-fifth the amount of N ingested. In a carnivorous animal like the dog, the digestion of bread seems to call for a much greater effort on the part of the pancreas than the digestion of meat or of milk (Walther).

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[1] With regard to Fig. 108 it should be said that the observations there represented were made before the discovery of *enterokinase*, and give therefore only the manifest trypsin content of the juice.

B. MORPHOLOGICAL CHANGES IN THE PANCREAS

Kühne and Lea observed directly on the *living rabbit* the changes which take place in the cells of the pancreas during secretion (Fig. 109). When secretion begins a change of form comes over the cells, which is expressed in a striking change of configuration of the tubule. While in the inactive state the latter appears perfectly smooth on the outer edge, during activity convex swellings which correspond to the separate cells become visible. The resting cells form an optically continuous picture within the tubule, but the active cells are marked off from one another by sharp and, for the most part, double boundary lines. Likewise during the active condition the striations in the outer zone, running from the base toward the inner border, stand out more clearly. The granules of the inner zone withdraw gradually from the region of the nucleus toward the lumen, become smaller and softer, and finally disappear altogether.

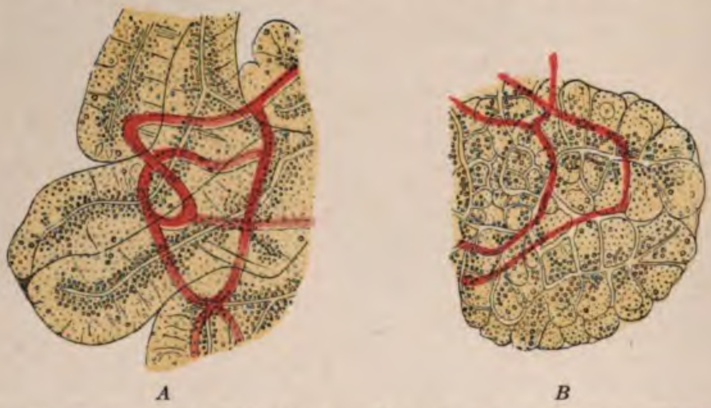

FIG. 109.—The pancreas of the rabbit, as observed in the living animal, after Kühne and Lea. *A*, resting state; *B*, secretion.

§ 5. THE LIVER AND THE SECRETION OF BILE

A. GENERAL PHENOMENA OF HEPATIC SECRETION

The secretion of bile differs from the other secretory processes thus far studied, primarily by being *continuous*, but also by the fact that, notwithstanding many researches, *secretory nerves* have not yet been found for the liver.

In this respect there is complete agreement between the bile and the urine, and one might suppose that these two secretory processes do not require the coöperation of secretory nerves, since in order to discharge their function of removing excretory products from the body they must go on continuously. As far as the kidneys are concerned, we know indeed that certain diuretic substances in the blood intensify the secretion of urine quite independently of the nervous system. It is possible that the same thing is true of the liver and that here, as probably in the kidneys, the regulation of secretion is the result of a vasomotor influence. However, this conclusion does not exclude the possibility of some controlling influence by secretory nerves, for experience with the secretory nerves of the stomach and pancreas teaches that the results of stimulation may be entirely masked by various different circumstances.

Although the secretion of bile goes on continuously, it shows certain variations which are not yet satisfactorily explained. Indeed the statements of facts themselves exhibit a difference in many points, which is but little gratifying. This much appears, however, from the observations at hand, that the *food exerts an important influence*. The quantity of bile secreted is least in fasting and declines steadily as the period is prolonged. The increase effected by the food depends in the first place upon the kind: meat causing a considerable increase, carbohydrates causing little or none at all.

Even in fasting the secretion of bile varies from hour to hour. After feeding meat the rise mentioned above does not appear at once, but, as a rule, only after the lapse of twenty to thirty minutes. The latent period is still longer after feeding fat. Statements disagree as to when the maximum occurs.

This long latent period is of great importance for our theoretical conception of the causes of the secretion, and seems to speak decisively for the view that the increase results from an exciting influence of substances absorbed from the alimentary canal, and that these substances act, therefore, directly on the liver. Whether this view actually represents the truth of the matter, or whether the increase in the secretion of bile which is to be observed after feeding is due to a reflex effect upon vasomotor or secretory nerves, must for the present be regarded as another open question.

The *direct stimulation of the liver* by bile-producing (cholagogic) substances is illustrated further by the following facts to which Schiff first directed attention. If both a biliary and an intestinal fistula have been established in a dog, and the bile obtained from the former be injected into the latter, or if ox bile be used for the same purpose, a considerable increase in the amount of bile flowing from the biliary fistula is obtained. Schiff explained these facts by saying that the injected bile was absorbed from the intestine, came to the liver and was again secreted.

We have direct proof of the correctness of this view in the fact that sheep's bile, when injected into a mesenterial vein of a dog whose hepatic arteries have been tied off, is secreted in the bile of the dog and can be demonstrated by the spectroscopic test for cholohematin, which occurs normally only in the bile of the sheep. At the same time the absolute quantity of bile rises. Bile or bile salts given by the mouth have the same effect. The percentage content of solids rises at the same time (Spiro and Voit).

B. DEPENDENCE OF THE SECRETION OF BILE UPON THE BLOOD SUPPLY

The *supply of blood* to the liver manifestly influences the secretion of bile to a considerable extent. If the general blood pressure be reduced markedly by bleeding, the quantity of bile secreted is diminished; at the same time, however, the percentage of solids increases. Cutting down the supply of blood by tying off several branches of the portal vein likewise diminishes the secretion. And when the vena cava inferior is compressed—so that the volume of blood passing through the liver in a unit of time is materially reduced—the same result is obtained.

The secretion of the bile declines on stimulation of the spinal cord, because of excitation of the vasoconstrictor nerves to the abdominal viscera, and a consequent fall in the blood supply to the liver. Section of the cervical cord produces a general fall of pressure throughout the vascular system and is accompanied by a decline in the output of bile. The output, on the other hand, increases after section of the splanchnic, because, in spite of the fall in general blood pressure, the blood supply to the liver increases on account of the dilatation of the portal vessels.

These and other kindred facts can be fully explained by variations of blood supply and contain no proof whatever that the secretion of bile is directly affected by secretory nerves. It is possible also that the rise of the secretion mentioned by some authors as beginning shortly after the ingestion of food, is produced by the dilatation of stomach and intestinal vessels during digestion.

We may summarize the facts thus far discussed as follows: The liver secretes bile continuously. This secretion is intensified by abundant supply of blood, also by certain bile-producing substances, especially the digestive products of proteids. There is yet at hand no single observation which would permit us to speak of any influence of secretory nerves on the liver. Like the other digestive fluids, bile represents an elaborated product of the secreting cells of the gland, for its specific constituents do not occur in the blood. The secretion pressure of the bile also is higher than the blood pressure in the portal vein.

Since the liver receives blood from several sources (hepatic arteries, portal vein and by return flow from the inferior vena cava), it is of interest to inquire whether any one of these vessels is indispensable to the production of bile, or whether all three can maintain the secretion independently. On closing off the hepatic arteries, secretion still takes place in abundance. Likewise after ligation of the portal feeding one of the lobes of the liver, the arterial branch supplying the same lobe alone mediates the secretion. Eck has shown that by an operation (Eck fistula) the portal blood can be conducted directly to the inferior vena cava, thus evading the liver altogether; and Stolnikow has found that secretion of bile continues after such an operation. This secretion occurs at least in part at the expense of blood flowing backward in the hepatic veins. For if the hepatic artery is tied off after the new route for the blood is established, the secretion still continues. It ceases however when the hepatic vein in addition is tied. Either kind of blood therefore seems to be sufficient to produce bile.

The hepatic artery supplies the gall bladder, the bile ducts and the interlobular branches of the portal vein with blood through its *vasa nutritia*. When these are ligated and the arterial blood supply thus completely stopped, multiple necrotic foci make their appearance in the liver. From the larger foci cysts develop; the smaller ones become transformed into connective tissue, and are followed finally by an hepatic cirrhosis.

When the discharge of bile into the intestine is prevented, the bile is reabsorbed. It does not pass directly from the biliary ducts into the blood, but is taken up, in part at least, by the lymphatic vessels. If the thoracic duct as well as the bile duct be tied off, it may happen that no constituents of the bile will pass into the blood (Harley); but there are statements to the effect that even under these circumstances they may find their way into the general circulation (Wertheimer and Lepage).

C. THE DISCHARGE OF BILE IN DIGESTION

When digestion is not going on the secreted bile collects in the gall bladder; there it loses water and becomes thicker. Neither bodily movements, nor movements of the alimentary canal, fasting, nor appetite have any effect in causing the gall bladder to empty its contents: the bile begins to flow from the bladder into the intestine only at the beginning of digestion.

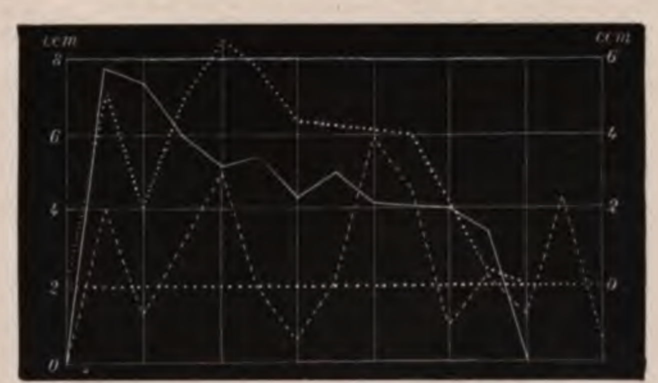

FIG. 110.—The hourly course of the discharge of bile into the intestine of the dog, following ingestion of different foods, after Bruno. ———— meat; - - - - - bread; . . . . milk.

The outflow of bile into the intestine is adapted to the immediate requirements by the following mechanisms. The discharge of bile from the ductus choledochus is controlled by a special sphincter. The gall bladder and the bile duct possess muscles which are under the influence of the splanchnic nerve. It is said that the duodenal sphincter of the ductus choledochus is innervated by the vagus. Phenomena witnessed on stimulation of the splanchnic show further that the gall bladder, as well as the ductus choledochus and the sphincter, may be reflexly dilated. Again by central stimulation of the vagus, reflex contraction of the gall bladder and relaxation of the sphincter may be produced.

The evacuation of the gall bladder and the discharge of bile in digestion, according to Bruno, are elicited by the passage of the stomach contents into the intestine. The substances active in this are the digestive products of proteids, extractives of meat and fats. The carbohydrates evoke no discharge of bile. Since the passage of the stomach contents into the intestine is governed by the kind of food, the discharge of bile is naturally different for different foods, as appears also from the diagram in Fig. 110.

With respect to the properties of the bile, it should be mentioned that the portions first discharged are thicker than that which comes later, because the former comes from the gall bladder, while the latter is freshly secreted.

§ 6. THE GLANDS OF THE INTESTINE

A. GLANDS OF THE SMALL INTESTINE

In fasting animals scarcely any secretion of intestinal juice takes place. But if the intestinal mucosa be stimulated directly, either by mechanical, electrical or chemical means, or if food be ingested, it makes its appearance. Whether an isolated loop of the intestine into which no food can pass begins to secrete without direct stimulation, must, in view of recent discoveries, be regarded as very doubtful.

If the nerve fibers running in the mesentery beside the blood vessels to an intestinal loop be cut, either immediately or after some time, an extremely abundant secretion appears in the loop, whereas the adjacent parts of the intestine outside of the tract deprived of its nerves show nothing of the kind. This secretion, which may reach the enormous value of one-eleventh of the body weight, continues for some hours, becomes somewhat scanty after four or five hours, but does not cease within twenty-four hours. At first the secretion is quite clear, containing no solid flakes, or at least only a few; but as time goes on the quantity increases so that finally a veritable "pap" is produced. At times the secretion is milky, like a thin gruel, and contains an abundance of intestinal epithelia (Moreau). Somewhat similar phenomena, more or less degenerative in character, make their appearance after extirpation of the cœliac plexus.

It is not easy to explain this secretion. We might regard it as primarily a transudation of fluid caused by the vasodilatation, and not as a true process of secretion at all if our knowledge of transudation in general did not speak decisively against such an explanation. If it were an actual secretion of the glands of Lieberkühn—a view which is confirmed by the properties of the fluid—it were easy to assume that the nerves whose section produced the hypersecretion exert a tonic influence which inhibits the glands. When the glands escape from this inhibitory influence they fall into the condition described. This hypothesis assumes that in the intestine itself conditions are present which would set the glands in excessive action, if they were not restrained by the nerves. But we know nothing more about it. Meantime let it be remembered as was remarked concerning the other digestive glands—the paralytic secretion of the salivary glands, etc.—that certain phenomena have been observed which point to such an inhibitory influence.

Other than this we have no knowledge of an ultimate influence of the nervous system upon the secretion of the intestinal juice. Vagus stimulation thus far has given only negative results.

So far as the few scattered observations on this subject go, the secretion of the lower part of the small intestine seems to be more abundant than that of the upper. It is stated also that the quantity of slimy flakes in the upper parts is greater. These flakes consist essentially of swollen cellular elements (epithelial cells and leucocytes) and of desquamated cells undergoing fatty degeneration.

If the two ends of an isolated loop of the intestine be sewed together and the intestinal ring thus formed be lowered into the abdominal cavity, one finds, when the animal is killed some months later, that the intestinal ring ***is filled full of a semisolid mass*** (Hermann). This mass, like the above-mentioned flakes in the intestinal juice, consists of dead cellular elements. It appears therefore as if cells of the mucous membrane perish in great numbers, even if, as in this case, no food or anything of the kind comes into the intestine. Nevertheless, this conclusion is not quite definitely established, for it cannot be maintained that the isolated loop is in a perfectly normal condition. And, in fact, Klecki has observed that if he washed the intestinal ring tolerably *free of Bacteria* with boracic acid and artificial gastric juice before sewing it up, and if in the further course of the experiment no pathological changes of any kind made their appearance, he found after the lapse of more than two months only a scanty deposit of yellowish, sticky, waxlike substance adherent to the surface of the membrane. This, like the contents mentioned above, consisted mainly of desquamated intestinal epithelial cells, but was by no means so abundant.

Histological studies of the glands of Lieberkühn have shown that their fundic cells have the same morphological character as the cells of the other digestive glands. Likewise in these the preliminary stages of the secretion appear in the form of granules which gradually increase in size and finally pass over into the secretion. These cells are very sharply distinguished by their properties from the mucous cells (goblet cells) of the intestinal epithelium (W. Möller).

B. THE GLANDS OF THE LARGE INTESTINE

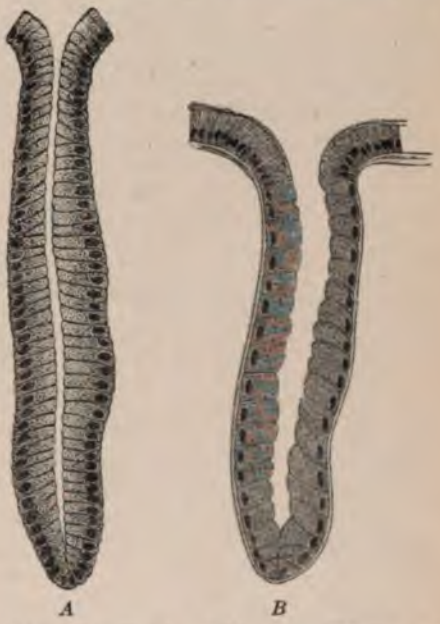

FIG. 111.—Glands of the large intestine of the rabbit, after Heidenhain. *A*, after very active secretion; *B*, after a long period of rest.

The glands of Lieberkühn in the *large intestine* do not secrete a digestive fluid. The properties of their secretion have been studied by making an opening into the large intestine and introducing various substances inclosed in small sacs of network. It has been found in this way that neither fibrin nor starch is digested. The secretion, which is but scanty, is a water-clear, odorless, thickly gelatinous and sticky mass of neutral reaction, containing turbid flakes of various sizes (Klug and Koreck).

The secretion of the large intestine, therefore, *plays no part* in digestion. The mucus contained in it probably serves to facilitate the passage of the intestinal contents which have become thicker by the absorption of water.

If the mucous membrane of the large intestine be studied under the microscope, after injection of pilocarpine into the animal, the glands are seen to be composed of cells which are strikingly like those of the glands in the small intestine. In alcoholic preparations the cells of both are small, longitudinally striated, and contain round or oval nuclei (Fig. 111, A). After prolonged rest the glands of the large intestine present quite another picture. The great majority of the tubes are clothed from base to mouth with cells which have gone through a process of mucous degeneration, and have taken the form of goblet cells—i. e., swollen structures with the nuclei in the basal end (Fig. 111, B). The contents of these cells behave exactly like those of the typical mucous cells (Heidenhain).

Likewise in the glands of the small intestine are found goblet cells between the true epithelial cells; but they are often wanting. Frequently they occur separately in the region of the upper end of the tube, rarely also at the lower end.

From these facts it follows that the cells during rest undergo *mucous degeneration*; in activity the mucus is discharged and the cell itself often perishes in the process. Just to what extent the latter takes place has not been finally determined. At the base of the epithelium are found here and there small round cells which are looked upon as substitutes for the cells which disintegrate.

THIRD SECTION

MOVEMENTS OF THE ALIMENTARY CANAL

§ 1. MASTICATION

The movements of mastication are for the purpose of dividing the food mechanically and of saturating it with saliva, so that a bolus may be prepared suitable for swallowing. Mastication is accomplished by movements of the lower jaw against the upper, the morsel of food being placed by appropriate movements of the tongue and cheeks, between the two rows of teeth, and being ground up by the latter acting against each other under the force of the powerful jaw muscles.

The teeth and the mode of chewing are unmistakably adapted to the kind of food eaten, so long as regard is had to the animals whose natural food is exclusively animal or exclusively vegetable. In man the teeth and movements of the jaw present no pronounced characteristics, doubtless because, with the assistance of the art of cooking, he has learned how to subsist upon so many different articles of diet. Raw meat cannot be properly reduced by the teeth of man; but if properly boiled or roasted so that the connective tissue binding the muscle fibers together is loosened, it is easily masticated. Likewise the seeds of cereals, which are otherwise incapable of being attacked by the human digestive apparatus, are rendered fit for food by boiling or by baking. Among all the articles of diet which are generally accessible to the higher animals, strictly speaking only grass and hay are incapable of serving man as food.

The actual grinding of the food is attended to primarily by the molar teeth, those in the front of the mouth serving only for biting off morsels of suitable size. The lower jaw is drawn upward by the masseter and temporal muscles, forward and upward by the internal pterygoids, forward by the external pterygoids. It is drawn downward by the digastric, the mylohyoid and the geniohyoid, and backward by the posterior belly of the digastric.

By contraction of the external pterygoid muscle of one side the jaw is moved toward the opposite side. In the depression of the lower jaw, the articular tubercle is moved forward in a line which is concave upward, at first slowly, then rapidly and at last slowly again.

The lips, cheeks, and tongue coöperate to bring the new or incompletely masticated portions of the morsel between the teeth, to facilitate saturation of it with the saliva and finally to form the mass into a bolus to be swallowed.

§ 2. SUCKING

The buccal cavity is capable of being closed air-tight. It can also be enlarged without admission of air, and in this way suction can be produced by which fluids may be drawn into the mouth.

When the buccal cavity is closed so as to be air-tight, the tip of the tongue lies against the teeth and the alveolar process of the upper jaw; the base of the tongue is raised on both sides against the back teeth and the neighboring parts of the upper jaw; the lower surface of the tongue rests on the edge of the lower jaw, and the soft palate hangs down loosely over the root of the tongue. Holding the jaws perfectly still with the parts in this position, a negative pressure of from 2 to 4 mm. of Hg. prevails in the mouth (Mezger, Donders). One can easily convince himself that the cavity is really air-tight, for if he depress the lower jaw without opening the mouth, the cheeks are drawn between the rows of teeth.

By drawing the tongue back or by lowering the jaw, the buccal cavity is enlarged and a suction is thus produced, which becomes still stronger if the tongue be drawn downward.

The space inclosed by the mouth parts in the act of sucking is about 77 c.c., three-eighths of which is due to the depression of the jaw, and five-eighths to the lowering and flattening of the tongue.

The power of suction in the human mouth is very great. It is possible by repeated efforts to develop a negative pressure of 700 mm. of Hg.

A child in nursing grasps the nipple of the breast with the lips in such a way that the mouth is closed air-tight. In the absence of teeth this is facilitated by special, membranous, and very vascular prominences on the edge of the gums of both jaws. These structures are found in the position of the four canines and, especially in the lower jaw, are united by a membranous seam projecting 1–3 mm. high.

§ 3. DEGLUTITION

We include under deglutition all those processes by which the bolus of food is propelled from the mouth into the stomach. It is a very complicated reflex process in which many muscles coöperate.

After the bolus is formed and is placed on the back of the tongue, the swallowing reflex is elicited by stimulation of the sensory nerves in the back of the mouth. In the ape the bolus, thrown into the pharynx, excites the reflex act in gliding over the tonsils (Kahn). In man no definite part of the mouth cavity from which the reflex can invariably be started has yet been made out. We can only say that it is induced when the bolus is forced back of the soft palate into the region of the tonsils. Thus far the process is under control of the will and the swallowing reflex therefore is inaugurated voluntarily, but thereafter it is independent of the will.

The first muscles to contract are the mylohyoids, and the pressure in the mouth cavity is raised by their contraction alone to about 20 c.c. of water. Almost at the same instant the hyoglossi contract causing the free surface of the base of the tongue, which in rest is directed backward and upward, to execute a movement backward and downward. By this contraction, according to Kronecker and Meltzer, fluid foods are spirted through the whole length of the œsophagus to its lower end before the contractions of the pharyngeal and œsophageal muscles can be brought to bear on them. Against this view, however, it may be observed that at the moment of the mylohyoid contraction the œsophagus is still closed by an elastic pressure exerted by the larynx. This closure is broken only when the larynx is drawn upward and forward, which takes place some 0.2 (Schreiber) to 0.3 of a second (Eykman) after the inception of the act—i. e., at a time when the effect of the mylohyoid is already past. If this be true, the movements of the above-named muscles of the tongue can only force the food mass into the pharynx (cf. Fig. 112, in which a sagittal section of the floor of the mouth and of the neck in both the normal position (A) and the open position (B) of the passageway is represented after X ray photographs; from B it is plain that the tongue in swallowing lies against the posterior wall of the throat).

When the food reaches the pharynx there follows in order the contractions of the pharyngeal and the œsophageal muscles. In the œsophagus the movement is executed at two different rates of speed. The muscle fibers in the cervical part of the œsophagus are cross-striated and the movement consequently is rapid; in the thoracic portion the cross-striated muscle layers are replaced more and more by smooth muscles and the movement of the food is consequently slower. The total time from the beginning of the act of deglutition until immediately before the opening of the cardia is about seven to eight seconds.

If the œsophagus be cut in the neck or even if a long piece of it be extirpated, and the superior laryngeal nerve, which very easily discharges the swallowing reflex, be stimulated, a perfectly regular act of swallowing results in which the contraction not only extends over the upper part, but appears just as usual in the part lying below the section (Mosso). The peristaltic wave of contraction therefore runs from above downward, under the direct control of the central nervous system. In deeply anæsthetized dogs this experiment does not succeed (Wild); but if in such animals the anatomical continuity be preserved, the contraction wave travels over the entire œsophagus. From this it follows that the contraction can be propagated through the œsophagus without the coöperation of the central nervous system, a circumstance which Meltzer supposes to be due to the action of peripheral reflex centers.

We have, therefore, to conceive the act of deglutition as taking place in such a way that once the reflex is induced, the different divisions of the passageway (floor of the mouth and tongue, pharynx, the various divisions of the œsophagus) are excited in a perfectly definite order by impulses coming from the central nervous system.

The nerves for the upper part of the œsophagus are found in the recurrent laryngeals, for the lower part in the pulmonary and œsophageal plexuses.

Since the pharynx is in open communication not only with the œsophagus but with the nose and the larynx, the pressure developed in swallowing might easily force the food into the wrong opening. But because of the different protective mechanisms brought into play this does not happen. The return of the bolus into the mouth cavity is prevented by contraction of the palatoglossal muscles, which approximates the tongue to the palate and narrows the isthmus of the fauces. This is assisted also by the styloglossal muscles, which raise the tongue and press it forward against the soft palate. The nasal cavity is shut off from the mouth and pharynx by elevation of the soft palate. When the palate muscles are paralyzed, water sometimes passes out the wrong way through the nose.

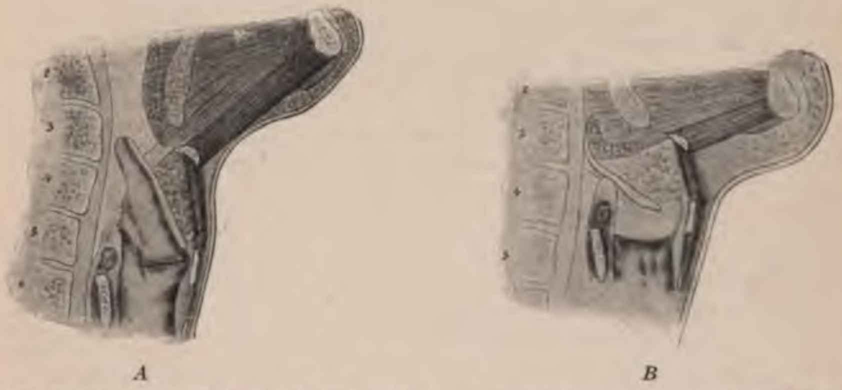
A B

FIG. 112.—Sagittal, optical sections of the floor of the mouth and of the neck, reconstructed from X ray photographs, after P. H. Eykman. *A*, position of quiet inspiration; *B*, position in swallowing; the passageway for food into the œsophagus is open. The observer is supposed to be looking into the left half of the larynx. In *A* the epiglottis is shown in the erect position. In *B* it is depressed, by the backward motion of the tongue, against the posterior wall of the pharynx (only the edge of the epiglottis is seen). In *B* the cricoid cartilage is raised to the upper border of the fourth cervical vertebra.

The larynx is raised in swallowing both for the purpose of releasing the pressure on the œsophagus so that it may be freely open, and for the purpose of preventing the passage of food into the larynx itself. This movement may be described as follows:

> The geniohyoid, mylohyoid and anterior belly of the digastric muscle draw the hyoid bone and the larynx, the lower jaw being fixed, forward and upward. The hyothyroid muscles serve to keep the larynx close up to the hyoid bone. At the same time the base of the tongue moves downward and backward, a movement already described as the effect of the hyoglossal and genioglossal muscles. By this means the cushion of fat which is found immediately over the epiglottis is pressed together from above downward, so that with the epiglottis it is pushed in as far as the bottom of the supraepiglottidean space, and the aryepiglottidean

folds are applied to the posterior side of the epiglottis (Fig. 112, B). The epiglottis itself cannot play any great part in the closure of the pharynx; for it can be extirpated without interfering with the act of swallowing. Nor do the muscles of the epiglottis appear to be of any importance.

This extremely complicated process of swallowing is in all probability presided over and controlled by the medulla. According to Marckwald the center lies lateral to and above the summit of the alæ cineræ.

When the bolus has reached the lower end of the œsophagus it is forced into the stomach. The cardia is normally closed by tonic contraction of its sphincter muscle, as is evident from the fact that no regurgitation of food takes place even when the pressure in the abdominal cavity is very greatly increased. The cardia is opened by the action of its dilator nerves (cf. § 4), and the bolus of food is pushed into the stomach by contraction of the lowermost section of the œsophagus. When the œsophagus is paralyzed by section of its nerves, food remains in it, and may be sucked into the lungs, producing inflammations which result fatally.

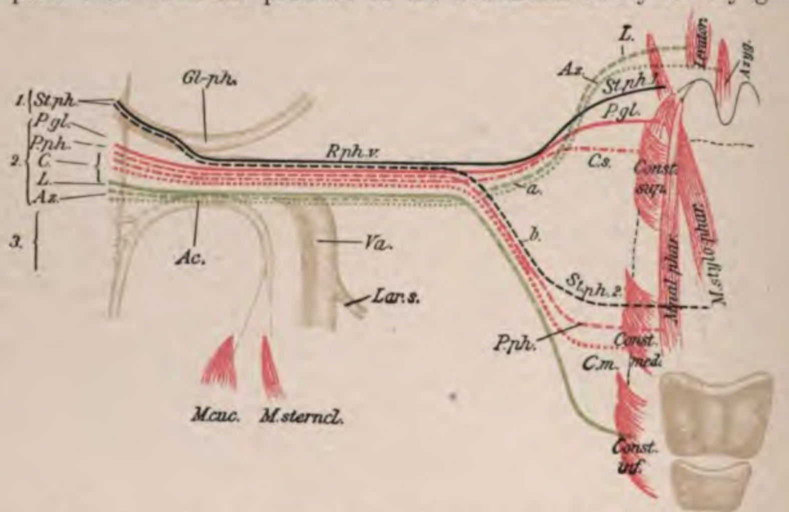

FIG. 113.—The motor nerves of the throat and palate of the monkey, after Réthi. 1, upper; 2, middle; 3, lower bundle of roots. *Gl-ph.*, glossopharyngeal nerve; *Va*, vagus; *Lar.s*, superior laryngeal; *Ac.* accessory nerve; *R. ph., v.* pharyngeal root of the vagus; *St. ph.*, the motor nerves of the stylopharyngeal muscle; *P. gl.*, motor nerves of the palatoglossal muscle; *P.ph.*, the motor nerves of the palatopharyngeal muscle; *C.*, motor nerves of the constrictor muscles of the pharynx; *L.*, motor nerves of the levator veli palatini; *Az.*, those of the azygos uvulæ.

By auscultation of the region over the cardia in man two sounds may be heard after deglutition, the one almost immediately after the inception of the act, the other some six to seven seconds later. The first sound is seldom heard and appears to be caused by an abnormal gaping of the cardia. In this case the food is probably spirted by contraction of the muscles in the upper passages, directly into the stomach. The second sound corresponds in its occurrence to the time when the food is being *forced* into the stomach, and it is probably caused by this procedure.

§ 4. MOVEMENTS OF THE STOMACH

A. KNEADING MOVEMENTS

The purpose accomplished by the movements of the stomach is to *mix the food with the gastric juice and to reduce it mechanically* by kneading and grinding. By this means the chemical changes to be wrought by the gastric juice are aided materially. The digestion of proteid in an artificial gastric juice requires much less time if the proteid is kept moving than if it is allowed to remain quiet. The proteid is more accessible to the gastric juice by reason of the movement, and the kneading, such as takes place in natural digestion, easily reduces to small pieces the masses already rendered brittle by the preliminary effect of the gastric juice.

With reference to the musculature of the stomach, we have to distinguish the two openings, the cardia and pylorus, as well as the main body or fundus, and the antrum pylori. The openings are surrounded by strong muscular fibers and are as a rule closed. The fundus, or body of the stomach, has a relatively weak musculature, the antrum a very strong one.

Observations on the movements of the stomach after the ingestion of food all agree in finding the *contractions of the pyloric portion* much more powerful than those of the body of the stomach. The former is marked off from the fundus by a ring muscle called the *sphincter of the antrum*. Relatively weak peristaltic waves sweep over the fundus from the cardiac end, and are continued by the very powerful contractions of the antrum, beginning at the sphincter of the antrum and spreading toward the pylorus.

Meltzer found that the fundic portion does not respond, even to very strong stimulation with easily recognizable contractions, whereas the pyloric portion with the same stimulus contracts more energetically the closer the stimulus is applied to the pylorus itself.

In a patient with a stomach fistula, a pressure of 14 to 35 mm. Hg. has been observed in the body of the stomach, and 130 mm. in the antrum. The antrum, it seems, may be closed off completely by contraction of its sphincter or by local contractions of separate sections, from the parts of the stomach lying to the left.

Since the pressure exerted by the fundic wall is commonly not very strong and the antrum is filled therefore during the dilatation which follows its own contractions under a very weak *vis a tergo*, the coarser portions of the food are probably not pressed into the antrum, but only the easily mobile, more fluid and more gruelly portions. If this is true, it follows further that the changes which the food undergoes in the body of the stomach are principally of a chemical nature, while the antrum represents the truly motor part of the stomach, where the bits of food already more or less comminuted are intimately mixed with the gastric juice and still more thoroughly ground up by powerful contractions.

Experiment shows that the stomach, deprived entirely of nerves, or even cut out of the body, undergoes *spontaneous contractions*; that like the heart, the stomach has, therefore, within itself all the necessary conditions of its movements—which is probably due to the ganglion cells found in the stomach wall (cf. page 288). But these movements are presided over and regulated in many ways by the central nervous system. The very complicated relations of the nerves concerned in this control will be evident from the scheme devised by Openchowski (Fig. 114).

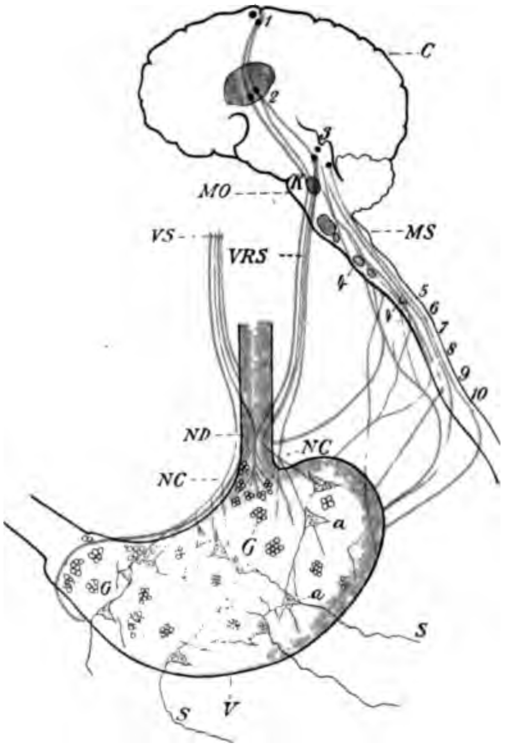

Fig. 114.—The nerves of the stomach musculature, after Openchowski. *Red*, the paths to the cardia; *blue*, the paths to the body of the stomach; *green*, the paths to the pylorus. *C*, the cerebrum; *V*, stomach; *MO*, medulla; *MS*, spinal cord; 5–10, thoracic roots; *VRS*, right vagus; *VS*, left vagus; *ND*, dilators of the cardia; *NC*, constrictors of the cardia; *a*, Auerbach's plexus; *S*, *S*, fibers from the sympathetic plexus. 1, sulcus cruciatus; 2, corpus striatum; 3, corpus quadrigemina; 4, centers in the spinal cord.

The stomach receives its *motor nerves* in part from the vagus, in part from the sympathetic nerves. These nerve paths have been followed up to the cerebrum as follows:

a. The *Cardia:* (1) From the region of the posterior corpora quadrigemina constrictor fibers run for the most part through the vagi; some run in the sympathetic paths, reaching their destination by way of the spinal cord and the fifth to eighth thoracic roots, thence through the two splanchnics. In the thoracic sympathetic the fibers are only sparingly represented. (2) The cardia is dilated by fibers which emerge from that region of the brain where the anterior lower end of the nucleus caudatus is united with the nucleus lentiformis, and join the vagus. In the spinal cord also as far as the fifth thoracic root, there are centers for the opening of the cardia which send their fibers by sympathetic pathways.

b. The *Body of the Stomach* between the cardia and the pylorus: (1) The brain centers for the contraction of this part, lie in the corpora quadrigemina, and the paths traverse both the vagi (chiefly) and the spinal cord, thence by way of the lower thoracic cord through the sympathetic trunks. (2) Inhibitory centers lie in the upper part of the cord and the paths traverse the sympathetic and splanchnics (according to Langley also the vagus).[1]

c. The *Pylorus and Pyloric Antrum:* (1) Contraction centers are found in the corpora quadrigemina for both the pylorus and its antrum. The chief path is the vagus, but the constrictor fibers run also through the spinal cord. (2) The dilator center for the cardia gives inhibition of the pyloric movements, but no opening. The path lies through the cord as far as the tenth thoracic root, then through the splanchnics. Inhibitory centers for the antrum are present in the corpora quadrigemina; and opening of the pylorus can be induced from the olivary body over a pathway which runs through the cord. The dilator nerve of the cardia under all circumstances proves to be a closing nerve for the pylorus. Opening of the cardia and contraction of the pylorus occur simultaneously. Langley finds inhibitory fibers for the pylorus also in the vagus.

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[1] Cannon has shown that distress inhibits gastric movements not only in the normal animal, but after the two vagi are cut, and after the four splanchnics are cut.—Ed.

B. EVACUATION OF THE STOMACH

When the stomach contents have been changed by the united action of the gastric juice and the movements of the stomach into a gruelly mass known as *chyme,* the object of gastric digestion is fulfilled; the pylorus is opened and the chyme is forced into the intestine.

The *length of time* the food is retained in the stomach depends to a great extent upon the kind of food eaten. In dogs having a duodenal fistula, Moritz has shown that pure fluids (water and uncoagulated milk) leave the stomach very quickly. With coagulated milk the evacuation is considerably slower. It is longest of all with the solid foods (meat, sausage). The consistency of the stomach contents therefore determines primarily when the food will be evacuated. But its chemical properties also are of considerable importance in this respect. The experiments of Moritz upon himself tended to show that water, weak salt solutions, and bouillon leave the stomach very quickly, but water containing CO_2, weak acid solutions, milk and beer remain considerably longer. If meat or bread be eaten the expulsion of water ingested at the same time is delayed considerably.

[Cannon fed fat, carbohydrate and proteid foods, uniform in amount (25 c.c.) and consistency and mixed with a small quantity of subnitrate of bismuth, to cats, and with the aid of the fluoroscope observed the rate of their discharge from the stomach. He found that fats remain longest in the stomach, proteids next, and carbohydrates a very short time. When carbohydrates and proteids were mixed in equal parts, the mixed food did not leave the stomach so slowly as proteids alone or so rapidly as carbohydrates alone. Fat mixed in equal amounts with proteids and with carbohydrates caused both these to be discharged more slowly than when each was fed alone.—Ed.]

Even with a diet of firm consistency, small portions having the consistency of gruel are forced into the duodenum as they are formed, and thus the evacuation of the stomach goes on gradually. It has been shown further that the pylorus closes and the expulsive movements of the stomach cease temporarily when a certain portion of the contents has been emptied (Hirsch, v. Mering). Not only the degree of fullness, but the reaction of the intestinal contents is of importance in this connection. A slight stream of HCl or pure gastric juice poured steadily through a fistula into the duodenum, will cause a soda solution previously introduced into the duodenum to be kept there for an indefinite time. A soda solution poured into the duodenum in the same way has no such effect. From this it follows that each outflow of stomach contents into the intestine stops further evacuation until the HCl of the gastric juice is neutralized by the alkaline fluids of the intestine (Pawlow).

C. VOMITING

Vomiting is an *abnormal process* by which the stomach contents are emptied through the cardia instead of through the pylorus. Several muscles are concerned in vomiting, but chiefly those of the diaphragm and abdomen. These contract all at once, producing a high intraabdominal pressure which naturally takes effect on the stomach wall. When the cardia is closed vomiting does not result. We know that this must be true because when simultaneous contractions of the diaphragm and abdominal muscles take place under other circumstances, for example in defecation, the stomach is not emptied through the cardia. The stomach wall itself plays little part in the process, for the entire stomach may be replaced by a swine's bladder and vomiting therefrom may be produced (Magendie). And yet it must be observed that the pyloric portion of the stomach contracts powerfully in vomiting and expels its contents into the fundus.

In vomiting the larynx and nasal passages are protected in the same way as in swallowing, and the mass of stomach contents ejected from the stomach under high pressure must therefore take its way through the mouth. The tongue is not raised as in swallowing, but is pressed down and held out in the form of a groove.

Vomiting is induced either by certain drugs or by reflexes set up from the base of the tongue, the throat, the stomach or the uterus. It may be caused also even by the imagination or sight of something nauseating, or by excessive disturbances of the brain.

As appears from the foregoing, a large number of muscles coöperate in the act of vomiting in a perfectly definite manner, and our current views of the action of the central nervous system make it very probable that this coördination is obtained by a special center (the vomiting center). In fact it is stated that in the dog the destruction of an area lying in the midline of the medulla in the region of the calamus scriptorius prevents vomiting—i. e., that this place is the vomiting center. This center is bilateral and lies in the deep layers of the medulla (Tumas). Whatever the facts as to the actual presence of such a center, this much appears certain, that the vomiting center and respiratory center are not identical, as has often been assumed. For while certain respiratory muscles take part in vomiting, many other movements supervene which have nothing to do with respiration. Besides, simultaneous inspiratory contraction of the diaphragm and expiratory contraction of the abdominal muscles never takes place in respiration.

§ 5. MOVEMENTS OF THE INTESTINE

The *purpose of the intestinal movements* is to mix thoroughly the contents of this division of the alimentary canal with the digestive fluids poured into its cavity, and to move the contents gradually along in the direction of the anus.

According to Grützner, antiperistaltic contractions occur normally in the intestine, by which the intestinal contents may be driven upward for some distance.

In the fasting state the intestine appears as a rule to be quiet. But about one-quarter hour after eating it begins to move. These movements are induced also by swallowing, by brief inhalations of ether, by psychic influences, application of cold to the abdomen and by direct stimulation (cf. *infra*).

Attempts have been made by investigation of intestinal fistulæ to determine the rate of propagation of the intestinal contractions, and different rates have been observed—which really was to be expected *a priori*, if one but considers how much the degree of fullness and the nature of the contents must affect the results. This consideration is confirmed by the observation made upon an exsected intestine, that a contraction locally produced is propagated along the intestine only when it is induced by the moving contents.

By observations on Vella fistulæ a value of 1 cm. in two to ten minutes, and 1 cm. in thirty to forty seconds, have been found for the rate of propagation of intestinal contractions, the latter value after ingestion of food. According to other observations the peristaltic wave would travel the entire length of the intestine of a dog in about ninety minutes. Again, the velocity of the intestinal movement has been estimated by passing a little balloon fastened to a string through a stomach fistula into the duodenum and measuring on the string the rate at which the balloon was forced along. In the uppermost parts the rate was greater than in the lower parts, and in the former reached the high value of 10–18 cm. in a minute. In view of the long time the food sojourns in the intestine this appears abnormally high.

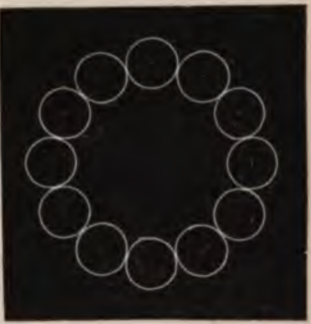

FIG. 115.—Schema to illustrate the relation of the longitudinal muscular fibers of the intestine to each other.

The intestine is of course constricted by the contraction of its circular muscles; it is shortened and at the same time dilated by contraction of its longitudinal muscles. Suppose, e. g., that in Fig. 115 the small circles lying side by side represent cross sections of the longitudinal muscle fibers. When they contract, they become thicker; each fiber therefore claims more space, and the fibers lying side by side becoming thicker all at once must have the effect of making the circumference larger—i. e., of dilating the lumen. This conclusion has been confirmed also experimentally (Exner).

With regard to the movements actually taking place in the intestine within the body, Cannon observed with the help of the Röntgen rays, after feeding a food mixed with bismuth subnitrate, that the food in an intestinal loop is divided all at once into small segments. From these segments new ones are continually being formed by *rhythmical contractions* [what Cannon calls "rhythmical segmentation"], at the rate of about thirty per minute. By this means the food is very intimately mixed with the intestinal fluids and is brought into close contact with the intestinal wall. The contents are then pushed along and the process is repeated over and over (Fig. 116).

The intestinal movements are to a certain extent *independent of the central nervous system*, for an exsected intestine may contract spontaneously. In animals whose nerves to the intestine have all been cut, two kinds of contractions may be observed.

(1) The intestinal loops execute *pendulum movements*—i. e., movements to and fro, in which the longitudinal, and, to a less extent, the circular

muscles are active. By virtue of the latter, small waves arise in the intestinal wall, which are propagated rather rapidly (2–5 cm. per second), usually from above downward.

(2) In separate parts of the intestine powerful contractions occur which proceed much more slowly than the above-mentioned small waves, but like them from above downward. These are the true *peristaltic movements.* In the propagation of these contractions the intestine is always dilated just below the place which at that moment is contracted.

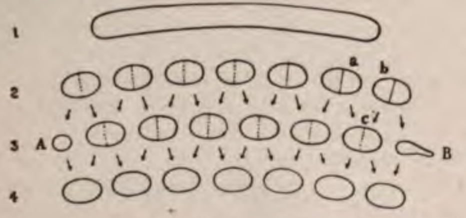

FIG. 116.—Schema to illustrate the rhythmical segmentation of the small intestine, after Cannon. 1, the contents of the intestine unsegmented; 2, the contents constricted into separate masses; 3, the next phase, the original segments are split in half by new constrictions and become fused into new masses, as *a* and *b* into *c*; 4, the first segmentation restored.

The peristaltic movements may be produced on an e-nervated intestine by a weak mechanical stimulus of the outer surface, or better still by the introduction of a balloon into the intestine. Every such stimulus *excites* the section lying above the point at which it is applied and *relaxes* that lying immediately below (Bayliss and Starling).

Peristalsis in the intestine is therefore a tolerably complicated phenomenon which calls for a definite, regular coördination of different portions of the intestine, and in all probability requires for its excitation the participation of a nervous mechanism. Since this can be observed in all its regularity both in an exsected intestine and in the intestine deprived of extrinsic nerves, the mechanism concerned must lie within the intestinal wall itself, and we have probably to regard the plexus myentericus as that mechanism.

Magnus is authority for the statement that the spontaneous movements continue unchanged in their character in surviving portions of the intestine, or in those preserved in Ringer's solution, after removal of the submucosa and of Meissner's plexus. But separation of the circular layers from Auerbuch's plexus stops their movements, whereas the longitudinal muscles left in connection with this plexus continue as before to contract. From these results it would appear that all the automatic movements of the intestine depend upon the action of Auerbuch's plexus.

The *intestinal movements are regulated* in many ways by the central nervous system; and we can say further that the small intestine receives its efferent nerves partly through the vagus and partly through the splanchnic. But with regard to the action of these nerves, until very recently there was absolutely no unanimity of opinion. Indeed one may say without exaggeration that every conceivable possibility has been represented by the different authors.

However, most authors now agree that the *splanchnics contain inhibiting fibers* for the intestine (Pflüger, 1857). If the abdomen of a fasting dog, having the splanchnics still intact, be opened, the above-mentioned contractions are not observed—the intestine is perfectly quiescent. A local stimulus is either entirely without effect or it produces only a circumscribed contraction. If now the splanchnics be cut, after some fifteen to twenty minutes the intestine begins to move as above described (page 288). These results show that the splanchnic under normal circumstances exercises a *tonic restraining influence* on the intestinal musculature. This inhibition appears still more clearly if the splanchnic be stimulated while the intestinal movements are in progress: the contractions immediately cease, and the tonus of the wall decreases.

Since the splanchnic conveys vasoconstrictor fibers for the intestinal vessels, it might be supposed that the cause of the intestinal calm following stimulation is to be found not in a specific inhibition, but in the resulting anæmia. But it is to be observed against this hypothesis that the necessary parallelism is wanting between the two phenomena. The increase in blood pressure is sometimes very considerable while the inhibition at the same time is only slight. The inhibitory effect is not evident at the first stimulation of the splanchnic and decreases with each succeeding stimulation, while the blood pressure goes on increasing. And finally, inhibition of the intestinal movements can be demonstrated even after the circulation is completely stopped by extirpation of the heart.

Many authors agree also that the *vagus is a motor nerve* for the intestine, while others have obtained no effect at all on the intestine by vagus stimulation. It is possible that this failure is due to the inhibiting influence of the splanchnics, wherefore it is recommended to sever the splanchnics first in such experiments (Jacobi). In order to prevent disturbances to the circulation resulting from stoppage of the heart by stimulation of the vagus, either the stimulation must be applied below the cardiac branches, or the latter must be paralyzed by atropine. Under such circumstances Bayliss and Starling and also Bunch have observed as the typical result of vagus stimulation, first a brief inhibition and then a contraction which becomes stronger and stronger. It would thus seem that the vagus contains both inhibitory and motor fibers, the former with a short and the latter with a long latent period. In the opinion of some authors these effects extend to both muscle layers; in the opinion of others the vagus inhibits the longitudinal fibers and excites the circular fibers (Ehrman, Winkler).

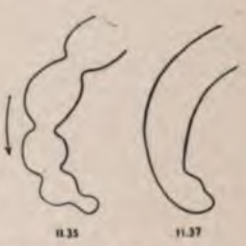

FIG. 117.—Schema illustrating antiperistalsis in the ascending colon, after Cannon.

As soon as the intestinal contents pass into the large intestine a powerful contraction of the cæcum and colon can be seen with the Röntgen rays (Cannon) to take place, and the contents are moved toward the rectum. A moment later peristalsis is succeeded by antiperistalsis, and the latter in rhythmical order now represents the usual form of movement of the ascending and transverse colon. Finally, however, it ceases, the contents collect in the transverse colon and are driven into the descending colon.

As for the innervation of the large intestine and rectum, Bayliss and Starling have shown that the former deprived of its nerves acts just as does the small intestine under the same circumstances. The vagus is said to contain motor fibers for the first part of the large intestine. The other parts and the rectum are supplied by the lumbar and the sacral nerves. The former arise from the second to the fourth lumbar roots, pass through the sympathetic to the inferior mesenteric ganglion and so to the intestine. The sacral nerves arising from the II–IV sacral roots traverse the so-called nervi errigentes (Langley, cf. page 233).

[According to Elliott the large intestine also receives inhibitory fibers from the sympathetic.—Ed.]

FOURTH SECTION

DIGESTION IN THE DIFFERENT DIVISIONS OF THE ALIMENTARY CANAL

Now that we have become acquainted with the properties of the different digestive fluids, and the processes by which they are formed, as well as with the movements of the alimentary canal, there remains yet for us to consider the *digestive process itself* in the different divisions of the canal, and to study the relative importance of each division.

By way of general remark it must be emphasized here once more that *appetite is of great and deep-seated importance* for the entire activity of the digestive apparatus. Only under its influence does a plentiful secretion of gastric juice take place immediately after the ingestion of food. The acid of the gastric juice in turn rouses the secretion of the pancreas which then without delay pours its secretion into the intestine; when, after a longer or shorter time, the stomach is emptied, the intestine is immediately prepared to continue the work of digestion and to carry it forward to the end.

Our knowledge of the conditions which control the movements of the alimentary canal are still too meager to permit us to say anything as to the importance of appetite and of eating for them. Certain observations of Pawlow show that desire for food does exert an actual influence on the movements of the stomach. Thus spontaneous movements of this organ are suppressed when the animal is greatly excited by the sight of food: the stomach is preparing itself for the reception of food (cf. also note, page 284).

§ 1. DIGESTION IN THE MOUTH

The most important function of the mouth with reference to digestion is the mechanical reduction of the food, and the admixture of saliva with it. Substances soluble in water are dissolved by the saliva and, what is more important, the morsel of food is rendered slippery by the mucin therein contained, and thus is the more easily passed through the gullet to the stomach.

The latter function is confirmed by the following observation of Cl. Bernard. An œsophageal fistula was made in the neck of a horse and the animal was given mouthfuls of wet oats. In one minute there came through the opening of the fistula 55 g. of the oats. After the ducts of the two parotid glands were cut off so as to shut out the saliva from the mouth, only 14.4 g. came through in one minute.—The mucus secreted by the glands of the pharynx and œsophagus also aids the passage of the bolus.

In several species of animals a diastatic enzyme is wanting in the saliva, and in these the physiological importance of saliva is restricted to the above-mentioned purely mechanical action. In general it has been supposed that even where the ptyalin is present the formation of sugar induced by it plays only a subordinate part in digestion, either because of the short time the food remains in the mouth, or because the swallowed saliva would quickly lose its diastatic power on account of the acid of the gastric juice. The latter conclusion presumes either that the acid content of the gastric juice is sufficiently high to neutralize the alkaline reaction of the saliva at once or that the stomach contents are very quickly permeated by the gastric juice. But neither presumption is warranted by the facts. Hensay has shown that as much as eighty per cent of the carbohydrates raised from the human stomach at the end of half an hour is maltose or the closely related dextrin. According to Cannon and Day, an acid reaction in the interior of the stomach contents of the cat can only be observed after one to one and one-half hours from the time of feeding, and during this time the ptyalin has every opportunity to act on the starch. This was confirmed also by direct experiments in which human saliva was given.

§ 2. DIGESTION IN THE STOMACH

The first division of the alimentary canal in which the food is chemically changed to any considerable extent, is the stomach. Here the carbohydrates are split up partly by the ptyalin of the swallowed saliva, partly by the acid and the Bacteria of the stomach contents. Starch paste is changed by the acid of the stomach to soluble starch, and from this with the help of acid fermentation under the influence of Bacteria, dextrin, sugar and lactic acid are formed.

Emulsified fat is split to a considerable extent by the stomach steapsin (cf. page 250). *Casein* is coagulated under the influence of the rennin, and the curd thus formed is dissolved again by the gastric juice. Moreover, what is of particular importance for the nourishment of children, almost the entire quantity of phosphorus from the curd passes, according to experiments *in vitro*, into solution in organic combination. The passage of the casein, which is the most important constituent of milk, into the intestine is delayed by its coagulation in the stomach.

The *pepsin-hydrochloric acid* dissolves all kinds of true proteids, the gelatin-forming substances and elastic tissues; but keratin is not acted upon. The influence of gastric juice on the gelatin-forming substances appears to be especially significant for the whole process of digestion; it is even said that they are dissolved more easily and more completely by the gastric juice than are proteids (Bikfalvi).

This is quite in line with all that we know about the function of the stomach. This function in brief is to transform the ingested food into a soupy mass, the chyme—to prepare it, in other words, for entrance into the intestine. The ability of the gastric juice to dissolve gelatin-forming substances aids in this direction; for the tissue elements which bind together the cells of the animal foods are composed of just such substance, and as soon as they are dissolved the cells are set free and the chyme is formed.

It is naturally a matter of great interest to determine how the transformation of proteid actually goes on in the stomach; for one can never form any definite conclusion about the cleavages actually taking place in life from experiments *in vitro* (page 244). Among the more recent contributions to our knowledge of this subject are the researches of Zunz on the digestion of meat in the stomach of the dog. At whatever time between one-half hour and six hours after feeding, the stomach contents were obtained, they consisted in by far the greatest part (eighty-six to ninety-eight per cent of the total nitrogen) of albumoses. Acid albumin was present only in small quantities and the total quantity of peptones, peptoids and end products only exceptionally reached more than ten per cent of the total nitrogen. Among the latter was found only a very sparing quantity of crystalline products, leucin, tyrosin, etc., and these might have been formed previously in the meat fed.

These results are to be explained in one of two ways: either the cleavage of proteid in the stomach proceeds only so far that about ten per cent of the proteid-N is transformed into end products, or the end products as they are formed are absorbed more rapidly through the stomach wall than the albumoses. It is not easily conceivable that the end products already in solution should pass into the duodenum more rapidly than the albumoses present in the same solution.

Looking to a decision between these two possibilities, Reach made experiments on surviving stomachs. The animals were killed at the end of the second hour of digestion; the stomach, tied off at both ends and cut out of the body, was maintained for four hours longer in a moist chamber at blood temperature. Since no absorption could take place, this experiment was well calculated to show how far the cleavage of proteid had actually gone. The result was that thirty-two to fifty-six per cent of the total N in solution (average forty-four per cent) was present in the form of albumoses, and fifty-six per cent in the form of peptones and end products, the latter alone containing some thirty-two per cent of the total nitrogen. It appears therefore that the reason for the ninety per cent and more of albumose nitrogen found in the intravital digestion is not that the enzyme action stops at the albumose stage, but that absorption going on at the same time removes the simpler products very rapidly.

Partly because of its hydrochloric acid, and partly quite independently thereof (London), *the gastric juice plays no small rôle as an antiseptic.* This property of the gastric juice is by no means sufficient to destroy all the Bacteria which find their way into the stomach; for very many are found throughout the alimentary canal, and in certain species of animals they play a very important part—of which more under the discussion of intestinal digestion.

Since the food always remains for a tolerably long time in the stomach, this organ most of all must suffer the harmful effects of an ill-adapted diet. We speak also of a digestible or indigestible article of food according as it is digested with greater or less ease in the stomach. It would be very important, therefore, if general rules could be established as to what is digestible and what is not. Unfortunately, however, this can be done only to a very limited extent, for the stomach is very capricious, and what is well suited to one stomach is unsuited for another.

Attempts have been made to determine the digestibility of different articles of diet and dishes by subjecting the stomach contents obtained from fistulous patients or from healthy individuals by means of the stomach tube, to investigation at certain intervals after eating. But it has been shown that in the same person the same food on different occasions requires a very different time for its formation into chyme. A presentation of these results would call for a discussion of a mass of details which would be out of place here. Besides, the fact just stated has lost much of its strangeness in view of the recent contributions on the conditions of secretion in the stomach (page 263).

Nevertheless, the following general principles as to the digestibility of a diet in the stomach may be laid down:

(1) A too voluminous meal is harmful to the stomach; for in order that it may be properly saturated with gastric juice, a very copious secretion—i. e., a great effort on the part of the gastric glands—is required, and in order to knead and mix it thoroughly, an unusual demand is made upon the stomach musculature.

(2) Poorly masticated or very compact food will likewise call for too great an effort on the part of the stomach; for the larger and more compact the pieces swallowed, the longer will be the time required to saturate them with gastric juice and dissolve them.

(3) Animal foods which are tough—e. g., meat from old, poorly nourished animals—are difficult to chew, and offer great resistance to the action of the stomach. The looser and more porous the food, the more easily is it digested in the stomach; a sick or weakly stomach, therefore, receives best a soft or gruelly food.

(4) Fat in the food has a great influence,[1] partly through its inhibitory action on the glands of the stomach. But not only so; if it permeates the food thoroughly, it forms a kind of protective film, which prevents the entrance of the gastric juice to the proteid or gelatin constituents. This is especially true if the fat eaten be not fluid at the body temperature.

(5) Strong spices, alcohol, etc., act unfavorably on digestion in the stomach, partly because, as with alcohol in great concentration at least, they reduce the action of the gastric juice on the food in some way or other.

(6) Digestion in the stomach is influenced also by other circumstances than the character of the food. Thus the digestive power of the gastric juice is reduced for a time by intense sweating, since both the HCl and the absolute quantity of the secretion are thereby diminished. Again exhaustion from intense muscular work causes a decrease in the quantity of gastric juice, which becomes thick, ropy and strongly mucous. It has even been observed that stomach digestion ceases entirely under heavy muscular work.

Since the function of the stomach is to change the food into a semifluid or gruelly mass, one might suppose *a priori* that the stomach could be dispensed with entirely, if the food taken were already of this gruellike nature. And this is in fact the case. The stomach has been successfully removed from dogs (Czerny), cats, and even from men suffering from carcinoma of the stomach, without endangering life or preventing digestion. It is only necessary to administer food in small portions and in a very finely divided state in order to maintain life as usual.

Our knowledge of gastric digestion and related phenomena show therefore that the essential function of the stomach, aside from the antiseptic action of the gastric juice, is that of transforming the food into a gruelly mass; but that its work can be replaced by careful comminution of the food before eating. And yet this rôle of the stomach is of very great importance; for it is owing to the gastric digestion that we can utilize all possible kinds of food for our nourishment, and can limit our eating to a few meals per day. If the food were to be introduced immediately into the intestine, we would be compelled to eat only fluid or semifluid foods, and it would be necessary to eat much more frequently than we do. More than that, the stomach protects the intestine from excesses of temperature whether high or low and from all kinds of harmful substances. It brings all the food to the temperature of the body and dilutes harmful substances with the gastric juice before allowing them to pass into the intestine. In short, the stomach is a protecting organ for the intestine, and permits us to derive our sustenance from a very great variety of foods.

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[1] See also page 285.

§ 3. DIGESTION IN THE INTESTINE

Comparative anatomy teaches us that the length and diameter of the intestine are intimately related to the character of the food of the animal species. In carnivorous animals the intestine is considerably shorter than in herbivorous animals; while in man its length is intermediate between these two extremes.

The *most important part* of the work of digestion is carried out in the intestine, and, as it appears, chiefly under the influence of the pancreatic secretion.

When the chyme enters the intestine from the stomach it is subjected to the action of this secretion, of the bile and of the intestinal juice.

The *pancreatic secretion* continues the transformation of proteids begun in the stomach. As we have already seen, the proteolytic enzyme of the pancreas is essentially different from that of the stomach. We may add to what was said before that the pancreatic juice acts rather feebly on the gelatin-forming substances (cf. page 291), whereas it acts very powerfully on the true proteids. This fact is in perfect agreement with the condition already emphasized, that the food must be of a gruelly nature in order to be adapted for digestion in the intestine. The proteolytic, the amylolytic and especially the lipolytic action of the pancreatic juice are assisted in some way not fully understood by the bile (Rachford and Southgate, Bruno, Ussow).

The action of pepsin-HCl on proteid is soon stopped in the intestine. In the first place the bile hinders the swelling of proteid necessary for pepsin digestion; moreover it has the property of precipitating proteids in acid solution, whence the pepsin is removed from the fluid with the precipitate. This precipitation of proteids by the bile can be very prettily demonstrated *in vitro*; but in natural digestion it appears to transpire only to a slight extent; for the bile-acid precipitate is easily redissolved by the bile salts, and by other salts like sodium chloride, lactate or acetate. It is stated also that one never finds any such precipitate in the intestine of an animal killed during digestion.

Hydrochloric acid in small quantities has no harmful effect on tryptic digestion and is even said to favor it in the presence of bile.

With regard to the *extent of digestion* of proteids in the intestine, Zunz has found that in the uppermost 50 cm. of its length the relative quantities of albumose and end products varies in favor of the latter, the longer digestion continues. After four hours, the nitrogen in the form of albumose amounts to seventy-six to ninety-five per cent of the total nitrogen; after six hours, seventy-one to eighty-three per cent; after eight hours, forty-four to forty-six per cent; and after ten hours, thirty-two to forty-four per cent. The end products increase therefore with the duration of digestion. We cannot draw from this any positive conclusion as to the form in which the digested proteid is chiefly absorbed, for it might very well be that the albumoses are more quickly absorbed from the intestine than are the end products. We shall discuss this question more fully in our study of absorption.

Proteid and its digestive products are attacked also by the *Bacteria* present in the intestine. To judge from observations on men with intestinal fistulæ, this action is only very slight; and this is probably the reason why the contents of the small intestine have no fecal odor. In the large intestine the Bacteria act much more extensively on the proteid, and as a result we find there besides carbon dioxide and marsh gas, sulphureted hydrogen, methyl mercaptan, skatol, phenol, etc., which give the fæces their characteristic odor. The bile pigments are destroyed in the large intestine by Bacteria, and bilirubin is changed into sterkobilin, which is probably identical with urobilin.

The putrefactive products arising in the intestine, which in so far as they are basic in character (like cholin and the different uric acid and creatin derivatives), are called *leucomaines*, are taken up by the blood and are there changed by chemical reactions into relatively harmless substances, and are finally eliminated in the urine. Formed in too large quantities and absorbed, however, they may remain in the body and cause a kind of poisoning, *autointoxication*, which produces more or less profound disturbances of the system.

Moreover, the body strives in many ways to *overcome all kinds of poisonous substances* which may be taken up with the food. Some are not absorbed from the intestine, some, as in the case of the different Bacterial decomposition products, are destroyed by the digestive fluids, some are retained and rendered innocuous by the liver and the mesenteric glands. It is plain that these processes, which cannot be discussed more fully here, are of the very greatest importance for the body, although the protection provided by them is not in all cases sufficient to save the body from poisoning.

Until recently it was rather generally assumed that fat is partly broken down by the pancreatic juice into the fatty acids and glycerin, that the former unite with the alkalies of the intestine to form soaps, and that the soaps bring about an emulsification of the fat. On account of its alkalies bile was said to play a prominent part. Unlike the other nutritive substances fat would then pass from the intestinal cavity into the mucous membrane, not in solution but in the form of an emulsion. The following two facts support this view: rancid fat is emulsified easily by alkalies, and the absorption of fats from the intestine is very considerably reduced by exclusion of the bile.

But by more exact investigation of the phenomena accompanying absorption of fat several facts have come to light which speak strongly against this conception. Free fatty acids are very well absorbed from the intestine even when their melting point is higher than 50° C. and when they cannot therefore become fluid in the body (I. Munk). The fine emulsion, known by the name of chyle, is in many cases entirely wanting from the intestine of the dog; and even when chyle is introduced into the intestine, the fine emulsion entirely disappears after three hours, and there is found now only larger fat drops surrounded by a turbid granular mass. *Lanolin* which is a mixture melting at 40°–42° C., made up of compounds of fatty acids with cholesterin, isocholesterin, etc., very difficult to split into their constituents, is not absorbed at all from the intestine of the dog (Cohnstein). Finally the histological findings in preparations of the intestinal mucosa made during absorption of fat are of such a character that they can scarcely be explained from the standpoint of the emulsion hypothesis (cf. page 304).

Against the emulsion hypothesis it has been observed also that in the dog the reaction throughout the greater part of the small intestine is acid in spite of very active absorption of fat; and in man the reaction of the small intestine is said to be acid. This reaction, however, is caused by an excess of organic acids and of carbon dioxide, and cannot be adduced as proof against an eventual formation of soaps (Moore and Rockwood).

In the light of these facts the emulsion theory cannot be looked upon as sufficiently well founded, and in fact another possibility is at hand to explain the absorption of fats. This is, that the *fats are completely decomposed* in the intestine and that the fatty acids formed are absorbed either as soaps or in a solution brought about by the bile.

This view, advocated especially by Altmann, Pflüger, Moore and Ratchford, and supported by many histological facts, is not contradicted by anything known concerning the extent of the decomposition of fats in the intestine, for that decomposition is in fact very great. To find, after feeding neutral fat, that some of it is not decomposed, of course proves nothing against the assumption, for the free fatty acids are absorbed as they are formed, and if the absorption goes on properly they might never be present in large quantity in the intestine.

It has been known since Strecker's time (1848) that bile and bile salts dissolve fatty acids quite easily. One hundred c.c. of dog's bile can dissolve 6 g. of mixed fatty acids from swine's fat, 5.5 g. from ox fat and 2 g. from sheep's fat. The solubility of the fatty acids in the bile depends therefore essentially on the presence of oleic acid, which has been shown also by direct experiment. The bile salts of themselves have a much smaller solvent power than the bile, among whose constituents lecithin must be the most important for this action. The solubility of soaps is increased also by the bile.

After exclusion of bile from the intestine, the absorption of fats declines considerably—a fact very easily understood in the light of the conception now under discussion. But even under these circumstances a certain quantity is absorbed, probably in the form of soaps. In the intestinal contents there is always found under normal circumstances more alkali than is necessary for the neutralization of the inorganic acids present, and there occurs as a consequence a certain amount of saponification. The soaps as they are taken up by the intestinal mucosa are again decomposed into fatty acids and alkalies, and the alkalies would then be at the disposal of the intestinal contents once more.

Likewise when the pancreas is extirpated, the utilization of fats is usually much diminished if not entirely stopped; fatty acids are then found in abundance in the fæces. The pancreas may be caused to waste away slowly, if its duct be ligated and 0.2 per cent sulphuric acid be injected into the gland. In this case the absorption of fat declines, but not to any considerable extent until a longer time has elapsed than in the case of extirpation. The cleavage of fat under such circumstances might be brought about either by the enzyme (formed in cells which are still functional) being absorbed and reaching the intestine by some roundabout way, or, as after extirpation, through the agency of Bacteria (Rosenberg). But the question is not yet finally settled.

If the conception here presented is in the main correct, then the principle upon which the transformation of foodstuffs in the alimentary canal proceeds would be the same for all, namely: they are changed by *hydrolytic cleavages* into substances which can be brought into solution by the fluids present in the alimentary canal, or by fluids poured into it from the glands.

The *carbohydrates* are changed into soluble carbohydrates principally in the intestine. The pancreatic juice plays the chief part in this, although it is assisted by the bile and the intestinal juice. Besides, the Bacteria present act upon the carbohydrates to a considerable extent. In this way, particularly in the small intestine, alcohol, lactic acid, acetic acid and succinic acid among other things (Nencki and his pupils) are formed. The acid reaction of the intestinal contents depends in part on these products.

The *intestinal Bacteria* have a very special part to play in the herbivorous animals; for by their agency cellulose is decomposed and the foodstuffs locked up by it are made accessible to the digestive fluids (Tappeiner).

The participation of Bacteria does not appear to be necessary in the digestion of animal foods, for various polar animals have no Bacteria at all in the intestinal contents (E. Lewin). Thierfelder and Nuttal have demonstrated the same thing for guinea pigs fed on milk and finely prepared vegetable food, such as cakes. Schottelius succeeded also in maintaining chicks for a time on perfectly sterile food. But from twelve days on the animals decreased in weight and died of hunger at about the seventeenth day. From this it seems that a coarse vegetable diet cannot be properly and continuously disposed of by the higher animals without Bacteria. And yet it must be added that the facts are by no means sufficient to warrant definite conclusions, for Lewin finds the intestine perfectly sterile in herbivorous polar animals.

In the lower animals enzymes (cytases) have been demonstrated which themselves destroy cellulose. The secretion of the snail's liver is an instance (Biedermann and Moritz; cf. page 110).

The *putrefactive processes* in the intestine are generally restricted within very moderate limits. The reason lies partly in the action of the hydrochloric acid of the gastric juice which reduces the number of Bacteria entering the intestine, and partly in the fact that the foodstuffs as soon as they are sufficiently digested, are removed by absorption from the sphere of influence of the Bacteria.

A very intense putrefactive process has often been observed in animals with a biliary fistula, and on this ground it has been assumed that the bile is a powerful antiseptic. But this conclusion is not correct; for in the first place it has been shown by direct experiments that bile is not a good antiseptic reagent, although it does exert an adverse influence on the development of certain Bacteria for a short time; and in the second place, animals with a biliary fistula which receive little or no fat but plenty of other food, do not, in spite of the diversion of the bile, experience any more putrefaction in the intestine than do normal animals. The loss of bile is therefore not of itself the cause of the putrefaction, when the diet is not exactly regulated. It is rather to be explained by the scanty absorption of fat; for when fat remains in the intestine as a foreign body, it affords a good culture medium for all kinds of Bacteria, which multiply prodigiously and produce an intense putrefaction, and through this a severe intestinal catarrh.

The same thing happens with new born children when they are fed with starches. The starch is incompletely digested in the intestine, it remains there as a foreign body and an offensive diarrhea develops, notwithstanding the presence of bile.

A large part of the small intestine *can be removed* from man as well as from animals, and digestion will not be interfered with to any considerable extent. After the removal of 3.1 m. of the intestine of a man, however, the intestinal evacuations were more abundant and the utilization of proteid was less than normal (Riva-Rocci). In the dog only slight permanent changes made their appearance, when as much as seventy per cent of the intestine was extirpated; although the diet had to be carefully regulated and an excess of fat especially avoided (Erlanger and Hewlett).

§ 4. FORMATION OF FÆCES AND DEFECATION

Digestion is continued in the *large intestine* by enzymes carried in with the intestinal contents. In the dog, digestion in this part of the alimentary canal appears to be of little importance, since complete removal of the large intestine reduces the absorption of foodstuffs but slightly. The proteids only are less perfectly utilized than normally (Harley).

In herbivorous animals the large intestine must play a more important part, for in the horse, for example, the cæcum is two to three times as large as the stomach. And yet rabbits from which the cæcum is removed live for months without showing any permanent disorder in the digestion or in the general health (Hultgren and Bergman).

The *chief function* of the large intestine is to provide for the absorption of foodstuffs capable of being absorbed which have not already been cared for by the small intestine, and by withdrawal of water to reduce the residue to a firmer consistency. The intestinal contents thus transformed are then finally voided from the body as the fæces.

The *fæces* contain some undigested constituents of the food, some unabsorbed products of digestion, putrefaction and fermentation in the intestine, dead intestinal epithelium and residues of the digestive fluids, and finally substances which are given off by the wall of the alimentary canal as excretory products (cf. pages 133, 308). The quantity of fæces evacuated daily varies somewhat according to the nature and quantity of the food eaten. With an ordinary diet it is estimated for the adult man at 120–150 g. with 30–37 g. dry substance.

The hardened masses to be removed collect in the large intestine and in the rectum, and are from time to time discharged from the body. The herbivorous animals (whose food is itself very voluminous, and in which the work of digestion goes on continuously) have frequent evacuations, notwithstanding the great diameter of the intestine. With carnivorous animals, whose food is very concentrated, the fæces are voided less frequently. Man ordinarily has one stool per day.

The intestinal contents are retained in the rectum by the tonic contraction of the two sphincters, the *sphincter ani externus* and *internus*. The sigmoid flexure of the descending colon has the effect of lessening the load to be borne by the sphincters. The action of the outer sphincter is strengthened by the levator ani, this muscle being thrown round the rectum like a loop.

The center for the external sphincter in the rabbit lies within the spinal cord in the region of the sixth to the seventh lumbar vertebra, in the dog at about the lower end of the fifth lumbar vertebra. Since this sphincter can be strengthened voluntarily, this center is also under the influence of the higher nerve centers. Contractions of the sphincters are obtained by stimulation of the motor zone of the cerebral cortex (dog). On the other hand, the tonus of the sphincters may be abolished by strong psychic excitation (involuntary defecation), and by stimulation of the motor zone of the cortex with the nervi errigentes cut (Frankl-Hochwart and Fröhlich).

From the spinal cord the *nerves to the sphincters* run partly in the hypogastric nerves and partly in the nervi errigentes, and in the dog the former are said to be inhibitory, the latter motor. Besides, the latter mediate contractions of the rectococcygealis and of the other longitudinal muscles of the rectum.

The tonus of the anal sphincters is not obliterated even by destruction of the spinal cord (Goltz and Ewald), a fact explicable in part at least by the presence of a center for the sphincter nerves in the inferior mesenteric ganglion (Frankl-Hochwart and Fröhlich).

Defecation is mediated by a reflex process not yet thoroughly investigated, which is induced from the rectum, and which is modified by influences of the will upon the muscles concerned. The sphincters relax and the hardened masses are discharged by contraction of the rectal musculature with the assistance of the abdominal pressure. The levator ani muscle may contribute to the general effect. By its contraction it presents a point of insertion for the longitudinal muscles of the rectum, and the compression of the rectum produced by it, coincident with the relaxation of the sphincters and the powerful effect of the abdominal pressure, assists in discharging the contents (Henle).

By *abdominal pressure* we mean the pressure upon the abdominal viscera produced by simultaneous contraction of the diaphragm and of the abdominal muscles. The part it plays in defecation depends upon the consistency of the contents of the rectum. If this is soft, defecation can take place without any assistance from the abdominal pressure; but with very solid excrement, the power of the intestinal musculature itself is not sufficient and the abdominal pressure is called upon.

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CHAPTER VIII

ABSORPTION

By *absorption* we understand all those processes by which the digested foodstuffs are taken up from the cavity of the alimentary canal into its mucous membrane and are forwarded thence to the general circulating fluids.

§ 1. ABSORPTION IN GENERAL

After Dutrochet had discovered the osmotic phenomena, it was thought that absorption in the intestine could be easily explained by osmosis. Digestion was for the purpose of changing the foodstuffs contained in the food into easily diffusible substances, if they were not already diffusible. Hence absorption took place according to the well-known physicochemical laws of osmosis.

More searching investigation, however, of matters as they are, have made us acquainted with facts which preclude so simple a process, and have led us for the present to the view that the *activity of the living mucous membrane* plays an essential part in absorption. It is perfectly evident that purely physicochemical processes, like filtration, osmosis, imbibition, etc., are involved, and this requires no further argument.

Among the more important observations for the theoretical explanation of absorption, those upon the behavior of weak salt solutions and of blood serum should be mentioned first (Voit, Heidenhain and others). If normal or slightly diluted blood serum be placed in an intestinal loop of a dog, notwithstanding that the conditions of the experiment exclude the coöperation of osmotic pressure, water and salts are absorbed in almost the same proportion as that in which they exist in the serum introduced, whereas the organic substances take part in absorption in far less proportion. If a solution of common salt whose osmotic tension is higher than that of the blood be introduced, according to the laws of osmosis no water should be absorbed; but it is absorbed. And, *vice versa*, common salt is absorbed from a solution in which the osmotic tension is less than that of the blood. The absorption of water from a weak dextrose solution is not changed, if the osmotic pressure of the blood be raised by intravenous injection of common salt (Reid). From equimolecular and therefore isosmotic solutions of different kinds of sugar which are stereoisomeric, the quantities of sugar absorbed in unit time are not equal (Röhmann and Negano).

Moreover it has been shown that the movement of salt in the normal intestine takes place in the direction from lumen to tissues, much more easily than in the opposite direction (O. Cohnheim); that an intestine cut out of an animal in full digestion, if bathed both within and without with a salt solution of the same strength, transports fluid only from the mucous membrane outward and not in the reverse direction (Reid); that if the cells of the intestinal epithelium be injured functionally, but not, so far as can be seen, anatomically by poisoning with sodium fluoride, absorption is actually altered so that osmosis now brings about only an exportation of fluid from the intestine.

Finally, attention should be called to the discoveries mentioned at page 34 with regard to the permeability of animal cells for different substances. According to those results, the entrance of a substance into a cell would depend upon its solubility in the lipoid limiting layer of the cell, carbohydrates not being soluble therein. To surmount the difficulty which carbohydrates present, Hoeber supposes that the absorption of these and other compounds which do not penetrate such a membrane occurs only between the cells. Something of the kind might be true of substances which are taken up in very small quantities; but carbohydrates are absorbed by the mucosa so abundantly that this explanation appears to have little probability in its favor.

The *power of absorption* is very different in different divisions of the alimentary canal. In the stomach pure water is not absorbed at all. Sugar or peptone or salts (if concentrated) are absorbed from their water solutions in the stomach the more plentifully, the stronger is the solution. The water is absorbed also under these circumstances, and, as it seems, most actively from solutions of peptone. Absorption of water from peptone solutions increases with the concentration, while from solutions of sugar it decreases with the concentration (v. Mering).

In the upper part of the small intestine (jejunum), *sugar and fat* are absorbed more rapidly than in the lower part (ileum). On the other hand the water of sugar solutions is said to be taken up by the mucous membrane more slowly in the jejunum than in the ileum (Röhmann and Negano).

Correspondingly, under a pressure of 10 cm. of water for 1 cm. of length, about 0.7 c.c. of a six-per-cent salt solution was absorbed in one hour by the upper part of the small intestine of the dog, and 1.3 c.c. by the lower part, while in the large intestine under the same circumstances the amount was 2.1 c.c.

The large intestine appears therefore to be especially well adapted for the *absorption of water.* Organic foodstuffs also in easily absorbable form are taken up from the large intestine, as has been shown by experiments with nutrient enemas, in which a supply of as much as 1,200 Cal. per day has been maintained. It is to be observed, though, that the ileocæcal valve is not an absolute barrier to the passage of the contents back into the small intestine, and that a part of the nourishment might be absorbed there instead of in the large intestine. According to observations on men and dogs with fistulæ into the large intestine, carbohydrates are absorbed there best of all the foodstuffs; fats and proteids only to a slight extent. The salt content of the enema also appears to have a certain importance in promoting absorption.

All kinds of *locally stimulating substances* (e. g., spices) exert a remarkable influence on the absorption in the stomach and intestine. In the former alcohol is absorbed even to the last trace in two hours, and besides, it accelerates the absorption of other substances. Common salt, oil of mustard, peppermint, pepper, etc., have the same effect. The condiments therefore not only favor the secretion of the digestive fluids, they further the absorption of the digested foodstuffs. Whether this action is due to a stimulating influence of these substances on the absorbing elements of the mucous membrane, or to vasodilatation caused by them, must for the present be regarded as undecided, although in the opinion of the author the former supposition is the more probable.

Comparison of absorption in the stomach with that in the intestine brings to light this fact, which is important for our understanding of the gastric functions: that the *stomach tolerates* much more highly concentrated solutions of the foodstuffs than does the intestine. The stomach acts as a *reservoir* for the ingested food, in order that the gruelly contents, properly diluted, may be discharged into the intestine gradually. But the latter plays the chief part in absorption.

In this connection we may mention also the experiments of Ogata in which the absorption of proteid was investigated after meat feeding, once when the meat was fed by the mouth, and another time when it was brought directly into the duodenum through a stomach fistula. The nitrogen output in the urine was taken as an expression of the absorption. It was shown that after direct introduction of meat into the duodenum the N-output rose much more rapidly and exhibited greater variations than when the meat had first to undergo digestion in the stomach. The absorption of proteid therefore takes place much more rapidly when it is placed directly in the intestine, than when it must pass through the stomach. We have then to add to what we have already learned about the importance of the stomach, that in virtue of its function as a storehouse, the absorption of ingested proteid is distributed more uniformly than it would be otherwise.

§ 2. ABSORPTION OF CARBOHYDRATES

We have no exact information as to how the carbohydrates are removed from the intestinal cavity (cf. page 302).

That they are carried off chiefly by the blood vessels, and not by the lymphatics, appears to be shown by a number of observations. For example, after a meal rich in carbohydrates, the amount of sugar in the chyle is no greater than after one poor in carbohydrates, while the portal blood shows a considerable increase in the former case. On the basis of these results and of the location of the blood vessels in the villi, Heidenhain has made the general statement that all substances soluble in water pass for the most part into the roots of the portal vein. Only when the quantity of fluid is very great does any sugar enter the lacteals.

This conclusion is confirmed in its entirety by observations on a young girl who had a fistula in the receptaculum chyli, from which all the chyle flowed out of the body. In this patient it was found that not more than five-tenths per cent of the absorbed sugar was taken up by the lymphatics (I. Munk and Rosenstein).

§ 3. ABSORPTION OF FAT

Because of the ease with which fat can be demonstrated by micro-chemical reactions, much attention has been given to its absorption.

It has already been stated (page 296) that fat is probably not absorbed as an emulsion, but in the form of a solution of fatty acids effected by the bile acids, or in the form of soaps.

Since the chyle, even after feeding with free fatty acids, contains neutral fat almost altogether, and free fatty acids only in much smaller amount, and after feeding ethylesters of the higher fatty acids contains only triglycerides and not a trace of the esters fed (Frank), we may deem it fully established that the free fatty acids absorbed from the intestinal canal are *synthesized again to neutral fats* in the intestinal wall. This is confirmed by the observation that the intestinal mucosa at the height of digestion contains far more neutral fat than free fatty acids, and that on digestion of the finely divided mucous membrane with a mixture of soaps and glycerin neutral fat is formed.

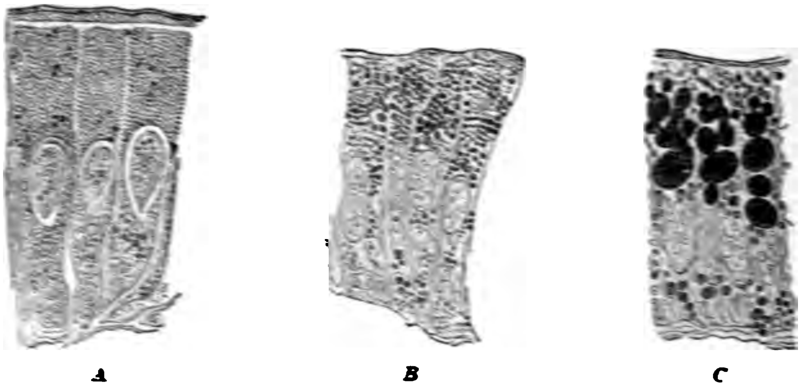

Fig. 118.—Successive stages in the absorption of fat in the epithelial cells of the frog's intestine, after Krehl.

This *synthesis*, like the absorption of fats from the intestinal cavity, is probably carried out by the cellular elements of the mucosa—possibly by the numerous leucocytes occurring therein, but more probably by the epithelium of the villi.

If the intestinal epithelium of the frog in different stages of fat absorption be studied in osmic acid preparations, all transitions are seen from small dustlike gray points to large, black fat droplets (Fig. 118, A to C). In the Mammalia the fat in certain early stages of absorption does not enter in the form of blackened granules, but of small black circles with a clear center. These circles increase in size and [illegible] in the further course of absorption—just the behavior we should expect if the fat were taken up as a solution of fatty acids and synthesized in the intestinal wall to neutral fat again.

With regard to the further fate of the absorbed fat, it is supposed that it is free to move inside the parenchyma of the villus only in the pericellular, fluid-filled spaces incompletely separated from one another by the connective-tissue trabeculæ of the stroma.

It has long been known that fat, for the most part, passes into the lacteals and is conveyed thence to the thoracic duct. Recent experiments have shown, however, that no small part of it passes also into the blood vessels of the intestine. In the case of the above-mentioned patient with a fistula in the receptaculum chyli, only about sixty per cent of the absorbed fat, and still less when free fatty acids were fed, was found in the chyle. Some forty per cent, therefore, had taken the pathway through the portal vein.

Besides the fatty substances absorbed from the food, other fats pass into the chyle, which have their origin in the intestine and its fluids. In this way, possibly, we may explain the fact that after feeding a fat of high melting point the mixture of fat in the chyle melts at the temperature of the body—i. e., that in the transition from intestine to chyle a lowering of the melting point has taken place.

When soaps are injected directly into the blood, they produce symptoms of weakened heart activity, the respiratory exchange of gases declines, the coagulability of the blood is abolished, and, with a dose of only 0.1 g. oleic acid per kilogram of body weight, rabbits are killed (I. Munk). The cause of these phenomena, according to Friedlander, lies in the fact that the calcium of the blood is precipitated by the fatty acids.

§ 4. ABSORPTION OF PROTEID

If the digestive enzymes continue to act long enough, the proteids are finally decomposed into simple crystallizable end products. To what extent this cleavage takes place in normal digestion, i. e., whether the proteid substances are taken up chiefly as albumoses or as crystalline end products, we cannot say definitely at present. It is possible, as some authors assume, mainly on the ground of the action of *erepsin*, that the cleavage of proteid, either in the intestine or in the mucous membrane, extends all the way to the final end products; but it is conceivable also that the albumoses, as soon as they are formed, are taken up from the intestinal cavity, and are not further decomposed in the mucous membrane.

The experiments of Voit and Bauer have shown that even native proteids in solution can be absorbed from the intestine without previous digestion. As much as fifty-eight per cent of egg albumin placed in a loop, isolated from the rest of the intestine, disappeared within five and one-half hours; twenty-eight per cent of blood serum in the course of one hour; etc. This however constitutes no proof that the first products would be absorbed in the course of normal digestion.

If blood be passed through the vessels of a surviving intestine, in whose cavity a peptone solution is contained, the peptone is absorbed but none of it can be demonstrated in the blood. From this, and from the fact that after a meal rich in proteid, the blood of the portal vein contained no more albumose than the blood of the carotid, it was concluded that the absorbed products of proteid digestion were changed in the mucosa to proteids of the same kind as those occurring in the blood.

But these experiments are not conclusive. If peptones are not to be found under the circumstances named, it might be due to further decomposition, and the discovery of erepsin makes such a view not improbable. The rapid rise of the N-output in the urine after feeding proteid shows that it is destroyed very soon after absorption. It would be a waste of energy if the body were to construct native proteids out of albumoses and peptones, only to destroy them immediately. The difficulty of obtaining a storage of proteid in the adult body also can be easily harmonized with its ultimate cleavage in digestion.

Direct observations thus far at hand are not by any means sufficient to establish a definite view of the matter. On the one hand, Cohnheim has found that one-third of a cat's intestine surviving was able to split 0.6 g. of peptone into its end products in two hours; on the other hand, Glaessner finds that albumoses are changed by the surviving mucous membrane into coagulable compounds; whereas Emden and Knoop reach the conclusion that in the surviving intestine taken while absorption of proteid was going on, there is neither a reconstruction of coagulable proteid out of albumoses and peptones, nor a cleavage of them into final products. They as well as Langstein state that from all appearances albumoses occur plentifully in the blood.

So far as the question can be judged at present, we might say that a part of the proteid eaten is absorbed as *end products of digestion*, another part as *albumoses and peptones*. How and where the latter are transformed into native proteids, and whether a synthesis of proteid from the end products can take place under any circumstances, cannot yet be decided.

Our knowledge is still unsatisfactory also with regard to the *manner of the absorption* of proteids. Hofmeister has supposed that the leucocytes of the mucous membrane are especially active in this, and the following facts among others appear to favor such an hypothesis. After meat feeding the lymph system in the small intestine of rats exhibits a larger number of cellular elements than after feeding lard or starch, but with the latter, more than in fasting (Asher). An hour after a meal rich in proteid, the number of leucocytes in the portal blood of the dog is considerably increased, and reaches a maximum probably during the third hour of digestion. This increase does not occur if the animal receives water, meat extract, salt, starch or fat, but no proteid. In proteid absorption, finally, the number of leucocytes in the venous blood of the intestine is greater than in the arterial blood (Pohl).

Some have sought to demonstrate an increase in the number of leucocytes in the skin capillaries of man after a meal rich in proteids; but this *digestive leucocytosis* is often wanting and is entirely denied by some authors. The possibility remains, however, that the leucocytes may take part in the absorption of proteids; for it is easily conceivable that the transportation of proteids from the intestine might be assisted by them, without their entering the general circulation in larger numbers.

The pathway which the proteids take in leaving the intestine is almost exclusively that of the portal vessels. In the fistulous patient above-mentioned (page 303) it was impossible after a meal rich in proteid to demonstrate any increase in the percentage of proteid in the chyle.

§ 5. ABSORPTION OF MINERAL SUBSTANCES

Since the easily diffusible salts, like sodium chloride, are absorbed by virtue of the activity of the epithelial cells this must the more be true of the heavy salts which diffuse slowly.

With regard to the behavior of different salts, Hoeber has shown that solutions of different salts isotonic with one another are absorbed at different rates. Since in these experiments solutions so dilute that the salts were almost wholly dissociated were used, their different behavior is to be ascribed to the properties of individual ions. Of the cations K, Na and Li are absorbed with approximately the same rapidity, NH_4 and urea more rapidly, Ca more slowly and Mg slowest of all. Of the anions Cl is absorbed most rapidly, then follow in order Br, I, NO_3 and SO_4. Now we know that the rate of diffusion of a salt in any given solution depends, first upon the degree of dissociation of its molecules, and secondly upon the velocity of migration of the ions. This law applies also in absorption; for the rates of absorption of salts are proportional to their rates of diffusion. However, parallelism between diffusion and absorption is subject to some limitations, which make other auxiliary hypotheses necessary and show once more that the physical factors are not sufficient to explain the behavior of the salts in the intestine.

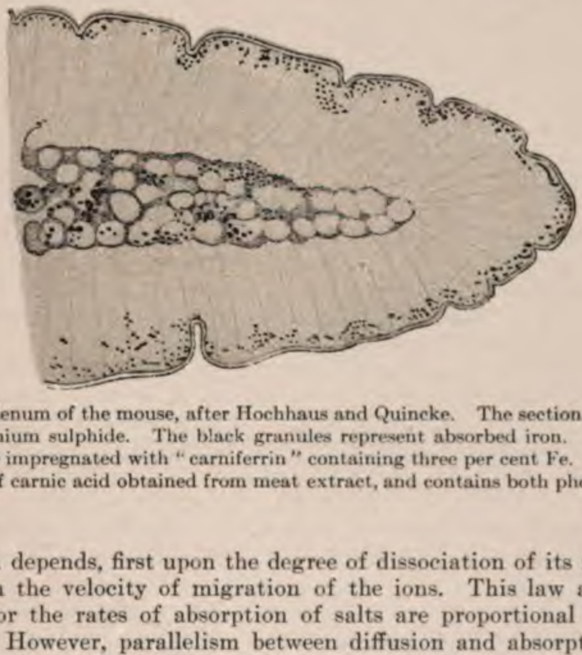

FIG. 119.—Duodenum of the mouse, after Hochhaus and Quincke. The section has been treated with ammonium sulphide. The black granules represent absorbed iron. The animal had eaten cheese impregnated with "carniferrin" containing three per cent Fe. (Carniferrin is a derivative of carnic acid obtained from meat extract, and contains both phosphoric acid and iron.)

In order to follow the absorption of water and of substances soluble in water more closely, a solution of methylene blue has been introduced into an intestinal loop and the mucous membrane studied microscopically. The pigment was found partly in the epithelial cells and partly between them, which means that absorption takes place here both between the cells and through them (Heidenhain).

The soluble salts, like the carbohydrates, are carried away from the intestine by the portal vessels; only in case the quantity of absorbed fluid is great does a part of it pass out by way of the lymph vessels.

The *absorption of iron* deserves special consideration. After it had been observed that very good results are obtained in the treatment of chlorosis by administration of different preparations of inorganic iron, and observers were pretty well convinced that these preparations were actually absorbed in the intestine, Bunge set up the doctrine that all the iron which is added to the blood and is the source of the iron contained in the hæmoglobin, arises exclusively from complicated proteidlike compounds, the *hæmatogens*, which are formed in the life processes of plants. Such compounds, resembling nucleo-albumins, occur also in egg yolk, etc. That iron preparations are certainly of great use in chlorosis, Bunge would not deny, but he explained the facts on the hypothesis that inorganic iron compounds in some way protect the organic compounds from decomposition in the intestine, and thus prevent the iron in them from being split off. Other authors have advanced other hypotheses, and attempts have even been made to explain the therapeutic effects of iron as the result of hypnotic suggestion.

However, it appears with greater definiteness from recent researches that the so-called inorganic iron compounds are absorbed in the intestine (Kunkel, MacCallum, Hall, Hochhaus, and Quincke *et al.*). A research carried out a short time ago by Abderhalden in Bunge's own laboratory shows the same thing, namely, that iron furnished in inorganic compounds, in hæmoglobin and hæmatin is absorbed even in small doses, and without destroying the complicated iron compounds. The absorption takes place through the activity of the epithelial cells (cf. Fig. 119). These cells then deliver the absorbed iron either to the leucocytes or directly to the blood stream.

Some of the absorbed iron passes into the thoracic duct (Gaule). According to MacCallum and Hall, if the amount of iron given be small, it is absorbed only in the uppermost part of the duodenum; with larger doses its absorption appears to take place in the lower parts of the small intestine, especially in Peyer's patches, and, according to Tartakowsky, almost throughout the entire extent of the gastrointestinal tract.

We have the following data with regard to the *further fate of iron* in the body. The iron contained in the body can be split off in part from its compounds by certain micro-chemical reactions (treatment with ammonium sulphide and ammonia, or with potassium ferrocyanide and hydrochloric acid); another part remains, however, in very stable compounds (e. g., hæmoglobin) in which it can be demonstrated only by their decomposition. The iron contained in these compounds represents the real iron stock of the body, other iron being in a state of transition and belonging either to the intake or the output of the body (Hall).

A part of the absorbed iron is used to renew or increase the supply of iron in the stable compounds, which may have been attacked in metabolism (hæmoglobin), a part is stored in the spleen, the liver and the bone marrow. In the spleen iron occurs as an inclosure within the pulp cells (Hall). According to Nesse, the iron compounds of the spleen represent products which have arisen by transformation of red blood corpuscles. The iron-containing substances of the liver are either nucleins (hepatin, Zoleski) or albuminates (ferratin, Schneideberg), or saltlike compounds (Woltering).

We have yet much to learn as to the way in which the artificial supply of iron affects the formation of hæmoglobin. It is conceivable that the iron is itself used in this formation, but it is also possible that the iron salts circulating in the blood stimulate powerfully the blood-forming cells of the bone marrow.

Even with food entirely free of iron, a *regular elimination of this element* from the body goes on, chiefly through the bile and through the mucous membrane of the stomach, cæcum, colon and rectum—although the separate portions of the intestine appear to participate to a different degree in different species. Elimination into the intestine appears to be accomplished by emigration of leucocytes and desquamation of epithelial cells. In certain animals the kidneys also take part in the process (Hall, Hochhaus and Quincke).

It is asserted by Raudnitz that the absorption of *calcium* and *strontium* takes place chiefly in the duodenum.

CHAPTER IX

RESPIRATION

THE function of respiration is to provide for an exchange of gases between the tissues and the external air. The blood in its circulation through the lungs takes up oxygen from the alveolar air and gives off to it gaseous products of decomposition, especially carbon dioxide. In order to renew the supply of oxygen and to free the alveolar air of decomposition products, a constant ventilation of the lungs is kept up by the respiratory movements. We have therefore to study first the movements of respiration and then the exchange of gases in the lungs.

FIRST SECTION

MOVEMENTS OF RESPIRATION

§ 1. ELASTICITY OF THE LUNGS AND INTRATHORACIC PRESSURE

The lungs are inclosed in an air-tight cavity—i. e., between them and the thoracic wall or the other organs contained in the thorax there is no air. Since the lungs are hollow sacs with elastic and easily distensible walls, it is obvious that they must dilate every time the thorax is expanded and must become smaller every time it is contracted. Since, further, the lungs are in open communication with the external air by the respiratory passages, it follows that in the former event air must be sucked into the lungs, and in the latter it must be driven out. The former phase of respiration is called *inspiration*, the latter *expiration*.

In the static position of the thorax, the entire atmospheric pressure takes effect through the air passages upon the inner surface of the alveoli. Indirectly through the alveoli the air pressure acts upon the inner wall of the thorax and upon the organs—heart, œsophagus, etc.—lying between it and the lungs. Since now the lungs are elastic, a part of the air pressure is expended in unfolding them, and the pressure taking effect upon the inner wall of the thorax must be less than the atmospheric pressure, by just so much as is necessary to expand the lungs. The intrathoracic pressure is therefore *negative*. Again, the more the thorax is dilated, the greater is the amount of the air pressure consumed in expanding the lungs, consequently the greater this negative pressure becomes.

The following methods have been used for determining intrathoracic pressure. A manometer may be connected terminally with the trachea of a corpse, and the thoracic cavity opened without injuring the lungs. Since the pressure within and without the lungs is thereby equalized, the lungs contract in virtue of their elasticity, the force of the contraction being measured by the pressure which the air column exerts on the mercury of the manometer. This is evidently equal to the pressure which was previously necessary to expand the lungs to their original volume. If the thorax were dilated more or less before being opened, the value of the pressure obtained on contraction would vary accordingly (Donders).

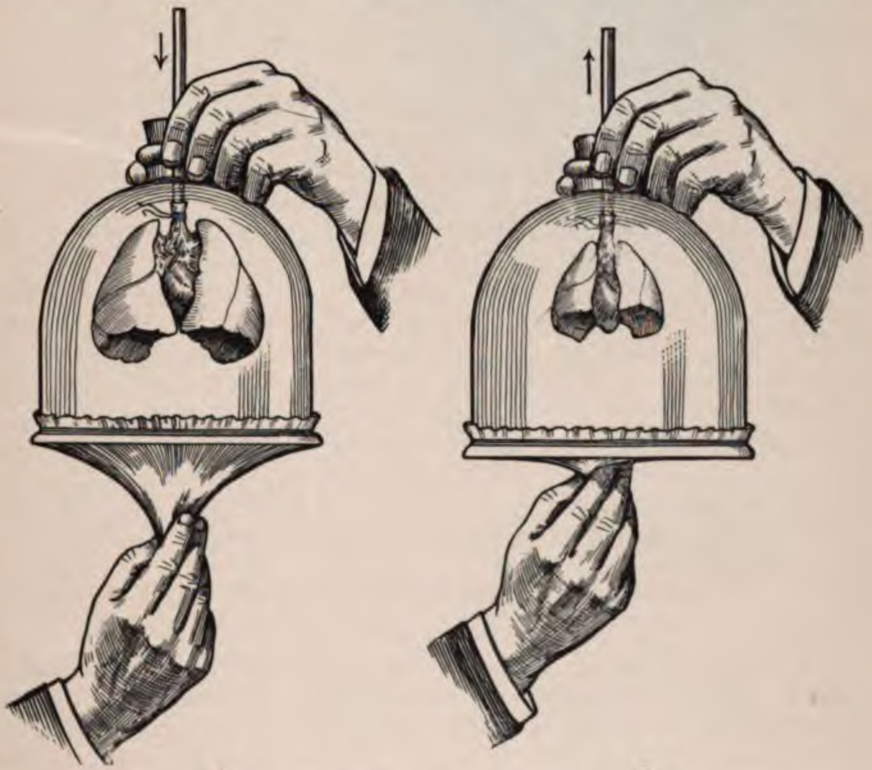

FIG. 120.—A simple experiment with the lungs of a rabbit to illustrate the normal expansion and collapse of the lungs in response to variations of the intrathoracic pressure. When the rubber membrane representing the diaphragm is drawn down (*A*) a negative pressure is produced inside the bell jar and the air enters the lungs through the glass tube tied into the trachea. When the membrane is released (*B*) the pressure inside the bell jar becomes less negative and the lungs collapse in virtue of their own elasticity, forcing the air out. The elastic recoil of the membrane, which tends to increase the pressure inside the jar, may be taken to represent the elastic recoil of the abdominal wall (cf. p. 317). A monometer can be connected through a second opening in the rubber stopper and the actual variations of intrathoracic pressure demonstrated at the same time.

The intrathoracic pressure can be determined on a living animal also, by introducing a flattened cannula through a slitlike opening into the pleural cavity, care being taken to prevent the entrance of air (Fredericq).

By the former method the intrathoracic pressure in man has been found to be: for the normal expiratory position, —5 to —6 mm. Hg.; for ordinary inspiration, in the neighborhood of —8 to —9 mm. Hg.; for deepest inspiration, —30 mm. Hg. Since the intrathoracic pressure rises immediately after death, these figures may be somewhat too low (van der Brugh).

With the glottis open the pressure in the pleural space is never positive. But when the glottis is closed and expiratory efforts are made so that the air in the lungs is compressed, the intrathoracic pressure may become positive. But in this case also the pressure within the lungs is greater than in the pleural spaces, for even now a part of the air pressure is consumed in unfolding the lungs.

The effect of suction in the thorax on the circulation has already been mentioned (pages 176 and 227). It plays an important part also in respiration. For the work to be done by the inspiratory muscles is considerably increased by this negative pressure, whereas expiration is favored by it. Thus since the air pressure acting upon the inner wall of the thorax is lower than the atmospheric pressure exerted upon the outer wall, every dilatation of the thorax is counteracted by a force corresponding to the difference between the outer and the inner pressure. If the pressure necessary to expand the lungs be taken as 8 mm. Hg., with an atmospheric pressure of 760 mm. the internal pressure would be only 752 mm. Hg. That is, the *inspiratory effort* at every movable point of the thoracic wall would be opposed by a pressure of 8 mm., and this resistance increases more and more as the expansion increases. It is obvious without further discussion that the *expiratory* contraction of the thoracic wall is favored by the same circumstances.

§ 2. INSPIRATION

The expansion of the thorax is accomplished in two ways: by *elevation of the ribs* and by *contraction of the diaphragm.*

A. REGISTRATION OF RESPIRATORY MOVEMENTS

Some of the methods in use are for the purpose of recording movements of the thoracic wall or of the diaphragm. The former can be registered either for man or animal by fastening a receiving tambour to the chest wall by means of a girth of suitable form, and transmitting the pressure variations accompanying the respiratory movements to a recording tambour. Fig. 121 represents a pneumographic curve obtained in this way.

Through a small hole in the upper part of the anterior wall of the abdomen a spoon-shaped instrument may be introduced between the diaphragm and the liver, and the movements of the diaphragm recorded by the movements which the instrument makes (phrenograph of Rosenthal).

By still other methods the volumes of inspired and expired air may be recorded. To this end tracheotomy is performed on the animal, and the trachea is connected with a receiver of suitable size (Fig. 122, B), which in its turn communicates with a recording tambour of Marey, or, better still, with a small spirometer (Fig. 122, A), or a similarly devised box known as an aero-

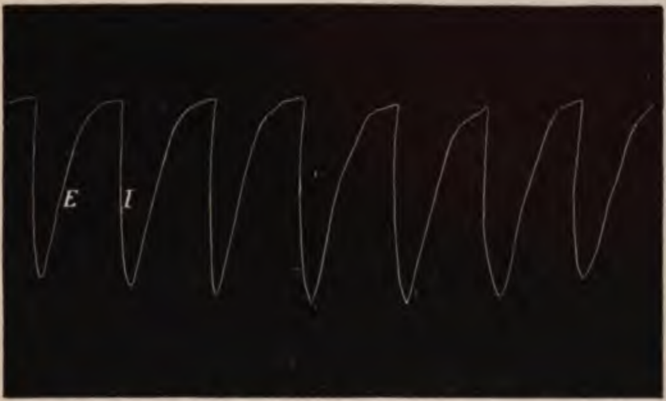

FIG. 121.—Pneumographic curve of a man, after Langendorff. To be read from left to right. *E*, expiration, *I*, inspiration.

plethysmograph (Gad). In Fig. 123 is reproduced a respiratory curve made with the apparatus pictured in Fig. 122.

The variations of intrathoracic pressure also are used for registration of the respiratory movements.

Finally, the respiratory movements can be recorded with the plethysmograph by placing the entire animal in a closed, air-tight box and allowing

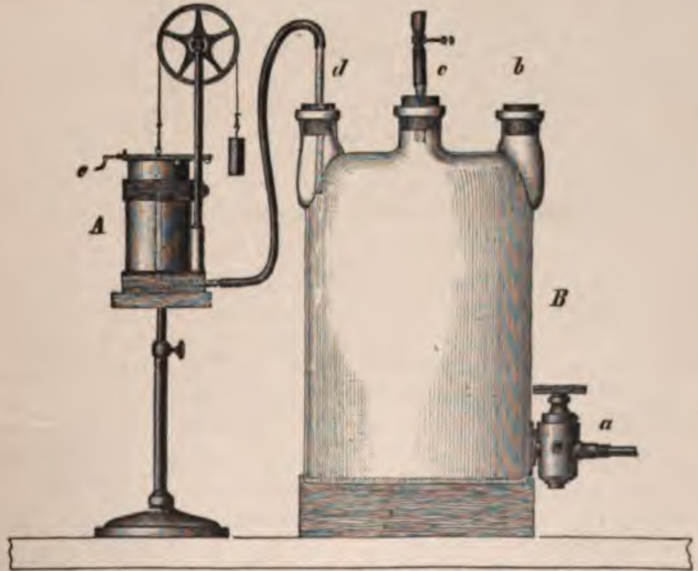

FIG. 122.—Apparatus for registering the volume of the respired air. *B*, receiver; *A*, spirometer; *e*, writing point. The trachea of the animal is connected with *a*. The openings at *b* and *c* serve to ventilate the receiver.

him to breathe through a tube opening to the exterior. The respiratory movements are represented by the variations in the volume of the inclosed air (Hering).

B. MOVEMENTS OF THE RIBS

The twelve ribs (Fig. 124) are thin, partly bony, partly cartilaginous hoops projecting from each side of the thoracic vertebræ, and bending outward, forward and downward, so as to inclose a space called the thoracic cavity. The upper seven pairs are fastened in front directly to the sternum along the midline of the body, while of the lower five pairs, two or three unite with the sternum indirectly and the others end freely.

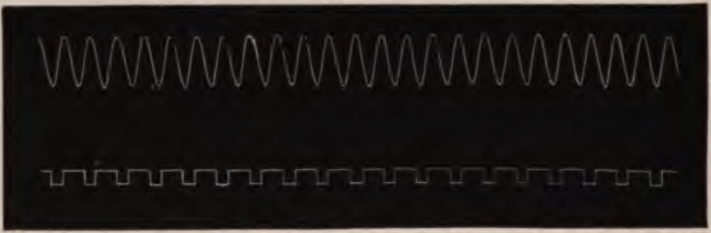

FIG. 123.—Respiratory curve of a rabbit. To be read from right to left. The downstroke represents inspiration. The lower tracing is a time record in seconds.

Each rib is joined to its vertebra by two articulations, one with the centrum, the other with the transverse process. Hence the axes around which the ribs rotate in their movements are determined by the relative position of the two articular surfaces. According to Landerer, the axes of the ribs from the first to the tenth lie in horizontal planes, but are not parallel, the angles which the axes make with the median plane being of unequal size. This angle for the first rib is about 80°, and decreases nearly uniformly from the first to the tenth where it is 44°. From this follows a fact very important for the study of the movements of the ribs, and which has been confirmed also by direct observation, namely, that the individual ribs by no means describe identical arcs. The axes of rotation of the last two ribs are inclined at angles of 10° and 20° respectively from the horizontal, while their intersecting angles with the median plane are 50° and 55° respectively.

When the ribs are raised on their axes, in the first place the distance of their anterior ends from the backbone is increased, and in the second place the lateral parts of the ribs are carried outward. The thoracic cavity is enlarged therefore in both the dorso-ventral and the transverse diameters. The extent to which this enlargement takes place at the level of the individual pairs of ribs depends upon the inclination of each and upon the intersecting angle it makes with the median plane. The greater the inclination, the greater, for ribs of equal length, becomes the dorso-ventral enlargement, and the smaller the intersecting angle of the axis with the median plane, the greater is the transverse enlargement.

In this elevation and projection of ribs the *sternum* is of course advanced, and this can only be accomplished by its rotation about a horizontal axis passing through the upper end of the manubrium. Since, moreover, the distances of the sternal ends of the different pairs of ribs from the spinal column are unequal, the separate segments of the sternum must be moved unequally and must be bent on each other; and, what is more important, the costal cartilages are thrown into a twist. Naturally this occasions some resistance to the elevation of the ribs, which, in addition to the resistance of their weight and of the negative pressure in the thoracic cavity, must be overcome by the muscles of inspiration.

If the ribs be moved out of their natural position by any force and this force then cease to act, they *will return of themselves* to the position of rest by reason of the above-mentioned anatomical circumstances.

Since, therefore, the elevation of the ribs causes an expansion of the chest, we shall designate as inspiratory all those muscles by the contraction of which the ribs are raised. This is not equivalent to saying that these muscles always act in inspiration. Some of the rib-lifting muscles, be it expressly observed, are active only in very exceptional cases, while in natural, quiet breathing only certain of the muscles participate.

The most widely different views have been expressed from time to time as to what muscles actually lift the ribs. This is especially true of the intercostal muscles. In the opinion of some, both the external and the internal intercostals are inspiratory muscles, in the opinion of others both are muscles of expiration; others again believe that the external tend to raise, the internal to depress the ribs; and finally, the view has been maintained that these muscles are present only for the purpose of regulating the tension in the intercostal spaces and of rotating the thorax in its long axis. By observations on living animals in which all the muscles of respiration were excluded except the intercostals, it has now been made clear that the outer layer, as well as that part of the inner included between the costal cartilages, serves to elevate the ribs, while the remainder of the inner layer draws the ribs down (Bergendal and Bergman, R. Du Bois-Reymond and Masoin, R. Fick).

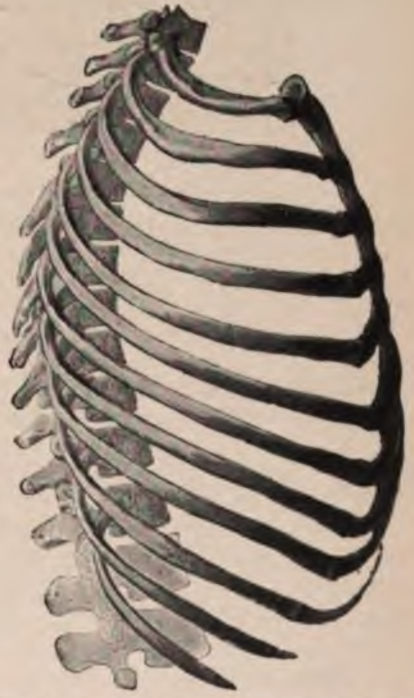

FIG. 124.—The thorax seen from the right side, after Spalteholtz.

In the rabbit at least the intercostal muscles are the most important so far as the thoracic breathing is concerned. When greater demand is made upon the muscles of inspiration, the *levatores costarum* and the *scaleni* are added first. The levatores alone are able to look after the respiratory movements for a certain time, and their action in the cat is very important (Koraen and B. Möller). Since these muscles are inserted quite close down to the hinder ends of the ribs, they can, with very slight contraction, produce very marked movements of the anterior ends.

In the rabbit with more vigorous respiration the *serrati postici superiores*, the *sternohyoidei* and the *sternothyroidei* come into play. In man, finally, Duchenne has found that in the greatest respiratory distress the following muscles are active: the *sternocleido mastoids* which lift the sternum when the head is fixed; the *pectorales minores* which lift the third to the fifth ribs with the scapula fixed; the *serrati antici magni*, the *pectorales majores* and the *subclavii*.

C. MOVEMENTS OF THE DIAPHRAGM

The *diaphragm* springs from the entire inner surface of the lower edge of the thoracic skeleton; its fibers converge toward the axis of the body, and attach themselves to the flat tendon situated in the center of the muscle. It presents a convex curvature toward the thoracic cavity, being, so to speak, arched over the convex upper surface of the liver.

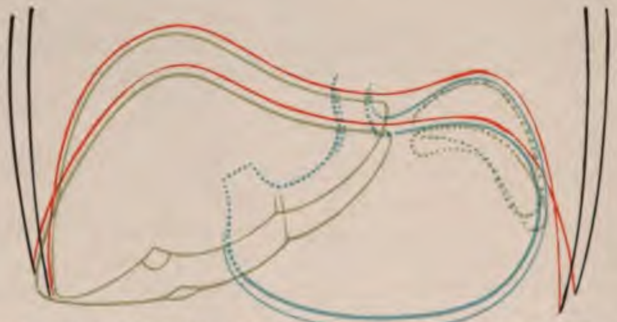

FIG. 125.—Schema, after Hasse, showing the movements of the diaphragm, liver, stomach, and spleen in respiration.

When the muscle fibers of the diaphragm contract, its dome-shaped upper part is flattened and moves downward. The central tendon takes part in the movement and becomes flattened because of the pull of the muscle fibers on all sides of its periphery. However, in deep respiration the dome itself always descends further than does the center (Hasse, Fig. 125). According to observations made with X rays (Cowl), during deep respiration the sweep of the diaphragm corresponds to the distance from the middle of the tenth to the upper edge of the twelfth thoracic vertebra. The maximal excursion of the central tendon is about 4 cm. (Grönroos).

At the same time by elevation of the ribs and of the sternum, the lower end of the thorax is increased in diameter (Duchenne). This is possible because the abdominal viscera, although depressed as an entire mass by the contraction of the diaphragm, present their upper surface as a fulcrum on which the circumference of the diaphragm is lifted. If the abdominal viscera be removed, when the diaphragm contracts the lower ribs approach each other and the lower end of the thorax is narrowed.

By reason of these changes the thoracic activity is enlarged from above downward and, at the extreme lower end, is enlarged also from side to side.

With regard to the *relative importance* of the diaphragm and the rib-lifting muscles in inspiration, we find among civilized people that in the man the diaphragm plays a more significant part than it does in the woman. Attempts have been made to relate this difference to the state of pregnancy and the attendant growth of the uterus. But this appears to be true only to a limited extent, for Sewall and Pollak have found that the respiration of Indian women is plainly of the abdominal type. The respiration of growing (European) girls is characterized by Gregor as a combination of the abdominal and the thoracic types, with the diaphragmatic part predominant, and with weak action of the shoulder girdle; that of boys as predominantly thoracic with strong action of the shoulder muscles. In forced respiration of boys the chief auxiliary mechanism called into play is the shoulder muscles, in girls it is the diaphragm. All this means that the actual cause of the feminine type of respiration, often considered as normal, is to be sought in the compression of the abdomen by clothes, especially the corset; and this has been confirmed directly by the observations of Fitz. As a consequence of this compression a woman gradually acquires the costal type of respiration, until finally it becomes normal for her.

We have at present but a single measurement of the absolute value of the diaphragmatic as compared with the costal enlargement of the thorax; namely, out of 490 c.c. of inspired air (in a man) about 320 c.c. devolved upon the elevation of the ribs and only 170 c.c. on the descent of the diaphragm (Hultkrantz).

§ 3. EXPIRATION

In ordinary quiet respiration the thorax appears to pass into the expiratory position principally by mere cessation of the inspiratory phase. When the diaphragm contracts it pushes the abdominal viscera downward and produces an increased tension of the abdominal wall. When it relaxes, it is brought back to its position of rest by the elastic recoil due to this tension. The ribs are brought back from the inspiratory position to their position of rest by the force of gravity and by the elasticity of the cartilaginous connections between the ribs and the sternum. Both in the abdominal and the thoracic types of respiration, the return to the expiratory position is aided by the elastic pull of the lungs (cf. page 311).

Ordinary expiration appears, therefore, not to require any muscular effort. The fact that expiration does not begin suddenly, but gradually, can be explained by saying that the contraction of the inspiratory muscles does not cease all at once, but rather slowly. According to some authors, however, the internal intercostal muscles, which, as we have seen, tend to lower the ribs, are active in ordinary expiration.

Under some circumstances expiration takes place by reason of muscular activity, and the volume of the thoracic cavity is diminished considerably more than is ordinarily the case. This kind of expiration is described as active to distinguish it from the ordinary or passive expiration. It is executed chiefly by the abdominal muscles.

By the contraction of these muscles (primarily the *recti* and *external oblique*, secondarily the *internal oblique*, and least of all the *transversi*) the ribs are drawn downward and the abdominal cavity is compressed so that the relaxed diaphragm is forced deeper into the thoracic cavity. In this way the thorax is narrowed as much as possible in all directions.

In Fig. 126 are represented according to Hasse two extreme types of respiration; in A a purely diaphragmatic type, and in B a purely thoracic type. In A no movement of the thoracic wall can be recognized, and the anterior contour of the abdominal wall only is projected in inspiration (*i*). In B the strong inspiratory movement of the thoracic wall forward and upward is evident. Because of the passive elevation of the diaphragm the anterior wall of the abdomen is at the same time drawn in; when the ribs fall in expiration the anterior abdominal wall curves forward again. The contour *i*, *i*, is the position of inspiration, the contour *e*, *e*, that of expiration.

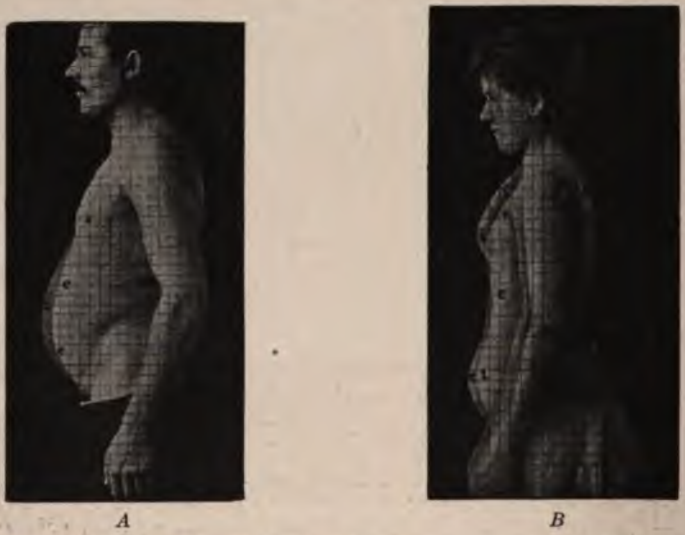

FIG. 126.—*A*, a purely diaphragmatic type of respiration. *B*, a purely thoracic type, after Hasse. *i*, *i*, the profile of the body in inspiration; *e*, *e*, the same in expiration.

§ 4. THE NUMBER OF RESPIRATORY MOVEMENTS

In quiet breathing the number of respiratory movements in the adult man is, on the average, 16 to 19 per minute; the extremes are about 11 and 24 (Quetelet). With younger persons the respiratory frequency is greater, being, for example, during the first year on the average 44 (maximum 70, minimum 23) per minute, and during the fifth year on the average 26 per minute (cf. Fig. 127).

Various circumstances, however, serve to alter the respiratory frequency. It is increased, for example, by muscular work (see below), by higher external temperature, or by an elevated body temperature, and may reach a very high value.

§ 5. EXCHANGE OF AIR IN THE LUNGS

The volume of air taken in with an ordinary inspiratory effort is estimated for the adult man at about 500 c.c. With a frequency of 16 per minute this would give a ventilation volume (breath volume, Rosenthal) of 8,000 c.c. = 8 liters, per minute.

According to Gregor, the average breath volume of children in the first month amounts to 1,300 c.c. per minute, in the twelfth month 3,000, and between the second and thirteenth years it varies between 4,000 and 5,000 c.c.

After an inhalation of the average volume, a considerable quantity of air can still be taken into the lungs, and after an ordinary expiration a considerable quantity can still be expelled from the lungs. But if we make the most extreme expiratory effort with the assistance of all the expiratory muscles, there remains in the lungs a certain quantity of air which, so long as the thorax is uninjured, can never be expelled.

This air left over is called the *residual air*. Attempts have been made, by various methods which cannot be described here, to determine its amount, and, if we neglect the values which are obviously incorrect, it has been found to vary from 500 to 1,600 c.c. We shall probably make no great mistake if we estimate it for the healthy adult man at 1,000 c.c. in round numbers.

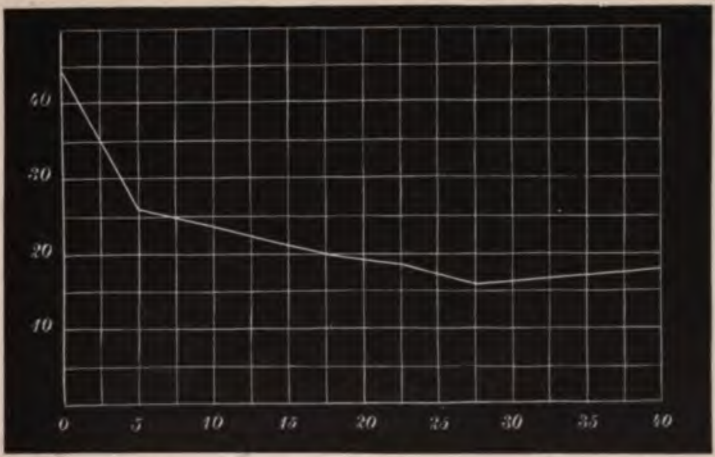

FIG. 127.—The number of respirations per minute in persons of different ages, after Quetelet.

The reason why the residual air cannot be expelled from the lungs is simply that when entirely collapsed the lungs inclose a much smaller space than does the thorax contracted to its smallest capacity. Since the lungs are pressed against the thoracic wall by the air inclosed within them, their volume cannot of course be diminished beyond the volume of the chest itself. When, however, the thoracic wall is opened, and the air pressure inside and outside the lungs is thereby equalized, they collapse in virtue of their own elasticity and drive out the contained air.

Even the collapsed lungs are not wholly empty of air; indeed, a lung which has once respired can never be entirely freed of its air by mechanical means. The reason of this is that in their collapsed state the walls of the smallest bronchioles press together and thus prevent further exit of air from the alveoli. This last quantity of air is spoken of as the *minimal air* (Hermann). That volume of air which can be expelled after an ordinary expiration amounts to about 1,600 c.c. and is called the *reserve air*. If after the usual tidal volume of 500 c.c. has been inhaled, inspiration be continued further, one can with the greatest possible effort of the inspiratory muscles take in some 1,600 c.c. more. This is called the *complemental air*. The sum of the complemental, the tidal and the reserve air (1,600 + 500 + 1,600 = 3,700 c.c.) represents the maximal extent of the exchange of air possible with a single complete respiration, and is called the *vital capacity* of the lungs.

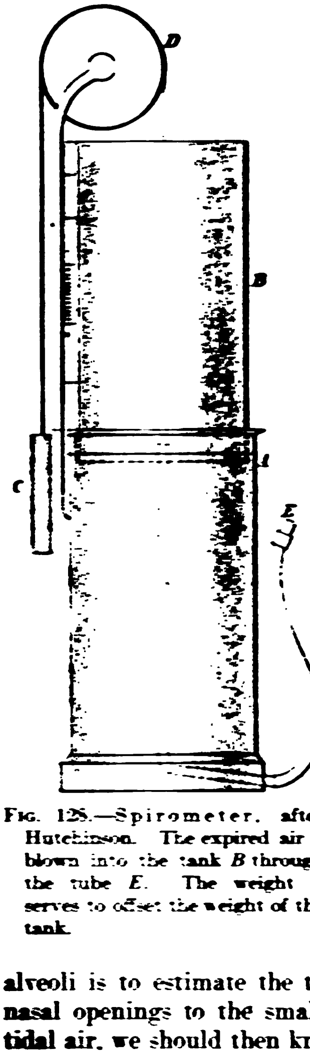

FIG. 128.—Spirometer, after Hutchinson. The expired air is blown into the tank *B* through the tube *E*. The weight *C* serves to offset the weight of the tank.

The vital capacity is measured by first taking as deep an inspiration as possible, and then exhaling with the help of all the expiratory muscles into a *spirometer* (Fig. 128).

From the facts thus far discussed we reach this important conclusion, that we always have the *power of increasing considerably* the quantity of inspired or expired air without exhausting the capabilities of the respiratory apparatus.

To be able to judge the effective result of pulmonary ventilation, it is of great importance to know whether the inspired air actually reaches the alveoli. The respiratory exchange of gases takes place in the alveoli; but the air which remains in the air passages, including the smallest bronchioles, can only contribute to this exchange by diffusion with the alveolar air, and, in view of the small diameter of the smallest bronchioles and of the frequency with which air in the passages is changed, this diffusion must be relatively insignificant. The only way to determine whether air goes directly to the alveoli is to estimate the total capacity of the respiratory passages from the nasal openings to the smallest bronchioles. Knowing already the volume of tidal air, we should then know whether the air passages alone were sufficient to commodate the tidal volume. Only two such direct determinations have t been made, but according to these the "noxious air space," as it has been led, amounts to about 140 c.c. (Zuntz). By an indirect method, the prinles of which cannot be presented here, the lower limit of this capacity is nd to be about 100 c.c. and the upper 150 c.c. (Loewy). Of the volume taken in at each inspiration the greatest part therefore reaches the alveoli. It is evident that this noxious space must exercise a greater influence, the more superficial the respiration.

§ 6. CONCOMITANT RESPIRATORY MOVEMENTS

Besides the muscles already considered as influencing the capacity of the chest, still others are active at the same time, which are of some importance for normal respiration.

Among these are the muscles which move the vocal cords. In quiet respiration the glottis is rather widely open and makes but slight movements (Czermak). But in more active respiration it is widened by contraction of the posterior *cricoarytenoid* muscles at each inspiration. When the muscles of the vocal cords are paralyzed, the cords take an oblique position with their upper surfaces directed outward. Their inner edges are thus separated but slightly from one another and, being relaxed, are drawn toward each other by the current of air. In young animals complete closure of the glottis may be produced in this way and suffocation be the result (Le Gallois).

§ 7. SPECIAL FORMS OF RESPIRATORY MOVEMENTS

The following are to be mentioned as special forms of respiratory movements: (1) *Coughing*, a powerful expiration produced reflexly and begun with a closed glottis, which is then opened by an explosive blast of air under high pressure, whence the accompanying sound; (2) *Sneezing*, a powerful reflex expiration, with open glottis and the mouth cavity closed off from the pharynx: it is often introduced by a deep inspiration; (3) *Laughing*, a series of short and weak expiratory blasts with lightly closed glottis; (4) *Yawning*, a deep inspiration with the glottis widely open, and as a rule with the mouth open; (5) *Sighing*, a deep inspiration followed by a prolonged expiration with partially closed glottis; (6) *Sobbing* is distinguished from sighing only by the velocity of the inspiratory act; it is usually accompanied by a spasmodic ascent of the larynx. All these forms of respiratory movements are produced reflexly, or are the accompaniments of psychical states and are even then to a certain extent reflex.

§ 8. PRESSURE CHANGES IN THE RESPIRATORY PASSAGES

On account of the slight force necessary to expand the lungs, when the thorax is enlarged they begin to expand immediately at the beginning of inspiration, and the alveolar air naturally is at first somewhat rarefied. With the glottis open new air flows in from outside; but in view of the relative narrowness of the respiratory passage and the constrictions occurring at different places along it, the inflow cannot take place instantly, and as a consequence one always finds a *negative pressure* in the air passages during the inspiratory phase. *Vice versa,* when expiration takes place, the air to be exhaled cannot escape immediately; hence we always find a *positive pressure* in the passages during the expiratory phase.

With an open glottis and a static condition of the thorax, the tension of the pulmonary air very quickly strikes a balance with that of the outer air, so that we meet the pressure variations just described only when the capacity of the lungs is being changed by inspiratory or expiratory movements.

In order to determine the absolute value of these pressure variations, a T-shaped cannula is introduced into the trachea of a dog, the animal breathes as usual through the uninjured glottis, and the variations of pressure are measured by a manometer connected with the unpaired limb of the cannula (Kramer). This method has been used also on patients with a tracheal fistula. With normal persons either the manometer tube is placed in one nostril and the subject breathes through the other (Donders), or he is allowed to breathe from a wide bottle connected on one side with a manometer and on the other by a wide tubulure with the outside air (Ewald).

It is evident that the values obtained in these experiments must be smaller, the nearer the manometer is brought to the outer openings of the respiratory passages. By the last-named method Ewald found a pressure of -0.1 mm. Hg. for inspiration and $+0.13$ mm. for expiration. When Donders placed the manometer tube in one nostril, he obtained for inspiration about -0.7 and for expiration $+0.5$ mm. Hg. In experiments on men with a tracheal fistula, Aron obtained below the glottis the value of -1.9 mm. for inspiration and $+0.7$ for expiration.

In order to measure the *force of the different phases* of respiration, a Hg. manometer is placed in air-tight connection with the mouth and nose by means of a closely fitting mask, and the subject breathes into the apparatus (Valentin, Hutchinson). Of course no air can pass into or out of the lungs, but instead the air already in them is rarefied or compressed according as the effort is made to inhale or exhale. The pressure readings given by the manometer may then serve as relative expressions of the power employed in the two phases. By such a method Hutchinson found in ordinary breathing a pressure of -50 mm. Hg. for inspiration and $+76$ mm. for expiration. With the deepest possible inspiration the pressure is given at something like -140 to -150 mm. Hg.; for the most intense expiratory effort possible the figures vary between $+108$ and $+256$ mm. Hg.

On three different individuals Mosso determined the inspiratory pressure for pure costal and pure diaphragmatic breathing and found the value in the former to be from -32 to -40 mm., in the latter from -10 to -20 mm. Hg. (cf. page 317).

§ 9. THE RESPIRATORY SOUNDS

By auscultation of the lungs and of the air passages, two different sounds can be heard; namely, (1) the *vesicular*, and (2) the *bronchial* sound.

To imitate the character of the vesicular sound one has only to suck in air through the mouth with the lips pursed: a sipping sound is produced which is almost exactly like the vesicular sound. It is said to be produced at the moment when the air current enters the alveoli.

During expiration there is to be heard in the normal condition of the thorax a weak and soft, indefinite aspirating sound which shows no trace of the sipping, vesicular sound of inspiration.

Over the larynx one can hear during both inspiration and expiration a very loud, sharp, aspirating sound in which *h* or *ch* is the predominating component. This laryngeal sound is propagated along the trachea and the two main bronchi, with gradually diminishing intensity (the bronchial sound).

§ 10. MEANS OF PROTECTION FOR THE LUNGS

The air passages leading to the lungs (nasal cavities, throat, trachea and bronchi) serve to protect the pulmonary alveoli from various kinds of injuries.

The narrowness of the nasal passages and the bend which the air passage makes in the pharynx serve the useful purpose of freeing the inspired air very largely of its dust particles since the latter adhere to the mucus-covered walls of one cavity or the other. This protection is largely wanting in breathing by the mouth. The dust particles are also driven outward by the cilia of the epithelium lining the air passages. This movement, especially in the parts below the larynx, is of great service in keeping the alveoli free of dust.

Of greater importance still is the fact that the parts of the respiratory passages below the glottis under ordinary circumstances do not permit the development of Bacteria: they are either entirely sterile or they contain an insignificantly small number of Bacteria (Jundell). Since the tracheal secretion possesses no antiseptic properties, this sterility must be accounted for in some other way as yet quite unknown.

Only in very exceptional cases does the inspired air have the temperature of the body; but the expired air comes out warmed to the temperature of the body and saturated with moisture. These changes occur chiefly in the wider passageways so that the bronchi and especially the delicate alveoli are protected from the harmful effects of loss of heat and loss of water. In fact, it has been found that when, by means of an aspirator, air at 10°–12° C. is taken in at one nostril and passed out at the other, entrance to the pharynx being closed, it comes out warmed to 31° C. and saturated with moisture. If the outside temperature be 0°–4° C., it is warmed to 27.5° C. In similar experiments with mouth breathing, the air reaching the pharynx was some 0.5° C. colder than with nose breathing (Aschenbrandt, Kayser). From these observations we are entirely justified in concluding that the air in the middle-sized bronchi at least has acquired the temperature of the body, and is immediately saturated with moisture at that temperature.

The closure of the larynx which takes place in swallowing (page 281) as well as different expiratory reflexes which are to be discussed in the following section are essentially for the protection of the lungs.

SECOND SECTION

INNERVATION OF RESPIRATION

§ 1. THE EFFERENT NERVES

Those muscles by the contraction of which the thoracic cavity is enlarged or diminished in size (if we neglect the purely accessory muscles) receive *their nerves* from the spinal cord: the nerves to the *scaleni* pass by way of the second to the seventh cervical roots; those to the *levatores costarum* and the abdominal muscles by the thoracic nerves; those to the *diaphragm* chiefly by the third and fourth cervical roots and the phrenic nerve. According to Luschka and Cavalié, the edge of the diaphragm receives some fibers also from the lowermost intercostal nerves.

If the spinal cord be sectioned below the exit of the last intercostal nerves, the operation evidently has no direct influence on the respiratory movements. But if the section be made in the thoracic cord, those muscles whose nerves emerge from the spinal cord below the section are paralyzed. After section above the first intercostal nerves, for example, the movements of the ribs, with the exception of those provided for by the scaleni muscles, cease entirely and the animal now breathes only with the diaphragm and the scaleni.

With still higher section of the spinal cord all the muscles above named are paralyzed and there remain only the movements of the glottis, the mouth and the nose (Galen, Le Gallois, Flourens).

When the diaphragm is paralyzed by bilateral section of the phrenics, various disorders in respiration appear, especially in animals which breathe mainly by the help of the diaphragm. These may be accounted for partly by the fact that the rib-lifting muscles now have all the work to do, and partly by the fact that since the diaphragm is now relaxed, the abdominal viscera are sucked into the thorax with each inspiration. However, no real danger to life is occasioned, if one is dealing with grown animals, which have a rigid chest wall and strong muscles. Young animals die after bilateral section of the phrenics, because the yielding chest wall and the immature muscles make it impossible to dilate the chest, once it has become narrowed by paralysis of the diaphragm.

Observations on men have shown that when all the muscles except the diaphragm are paralyzed, as well as when the diaphragm alone is paralyzed, life may be still maintained. In the latter case the respiratory frequency becomes greater than normal and breathing goes on, without any participation of the accessory muscles, under the coöperation of the *levatores*, the *intercostals* and the *scaleni*. Great bodily exertion, however, results in severe respiratory distress.

The *motor nerves* for the muscles of the larynx and bronchi run in the trunk of the vagus. Among the laryngeal muscles the cricothyroid is innervated from the superior laryngeal, the others from the inferior laryngeal.

It was asserted by Longet (1842) that the *bronchial muscles* also are under the influence of the vagus. This statement was often disputed by later authors, but it has been established by the newer, much improved technique that the vagi do in fact produce contraction of the bronchial muscles, and, especially in the cat, contain inhibitory fibers also for these muscles.

The bronchial muscles of the dog are under *weak tonic stimulation*, those of the horse under a strong tonus; they are influenced, feebly as a rule, by various afferent nerves, both contraction and relaxation appearing as the results of stimulation. The most important broncho-constrictor reflexes appear to be started from the mucous membrane of the respiratory passages (nose, larynx), and may possibly be regarded as protective reflexes, for the narrower the bronchi become the more likely is the dust of the air to adhere to their walls.

The chief service of the bronchial muscles is that when the intrabronchial pressure rises, they give by their contraction a greater degree of firmness to the bronchial walls.

The mucous glands of the larynx and of the trachea receive their nerve fibers through the *laryngei* nerves. In these also are afferent fibers which produce a reflex secretion of mucus in the larynx and trachea (Kokin).

§ 2. THE RESPIRATORY CENTER

Since in the movements of respiration a large number of muscles contract in a definite sequence, it is to be assumed in conformity with our present views of innervation, that somewhere in the central nervous system is a *center controlling these movements.*

From the fact that these movements do not cease when the brain is cut through as high up as the pons, it follows that the respiratory center must be situated below that point—i. e., *not higher than the medulla.* When such a section is made, the diaphragm stops for a moment, but begins of itself to contract, and continues quite regularly unless some unintentional lesion has occurred.

When, on the other hand, the medulla is separated from the spinal cord, respiration ceases. Galen knew that in the upper part of the spinal cord there is a place the destruction of which at once stopped respiration, and Le Gallois (1812) showed that this spot is in the medulla. For a long time it was generally agreed that the respiratory center was to be sought only in the medulla. Recently, however, it has been claimed with great positiveness that, although there is a regulatory apparatus in the medulla, the *true centers* for the respiratory movements are to be sought in the spinal cord, and the advocates of this doctrine go so far as to say that the nuclei of the respiratory nerves are stimulated simultaneously by the blood, thus giving the impulse for a coördinated respiratory activity (Brown-Séquard, Langendorff, Wertheimer). The stoppage of respiration after section of the cervical cord would, in their opinion, be due not to separation of the respiratory nerves from their center, but to the shocklike, inhibitory effect of the section.

There are numerous experiments which show that direct stimulation of the spinal cord with electricity or by mechanical means may stop respiration, and the view just mentioned is well supported by such facts. But it is at present impossible to decide how long such an effect of shock may last. If an animal whose cord has been sectioned in the neck be maintained by artificial respiration, it can be kept alive for hours. But if the animal still does not breathe spontaneously one cannot refute the claim that shock still persists.

In cases where artificial respiration is first maintained for a long time, rhythmical respiration has been observed on animals with the cord severed in the neck. Some of the first observations of this kind were made on newly born animals and some on animals whose reflex irritability had been artificially increased with strychnia (Rokitansky, Langendorff). Later Wertheimer succeeded in obtaining spinal respiration in grown animals which had not been poisoned. But when spinal respiration does appear it is never of the same extent as that controlled from the medulla, and it continues, so far as is yet known, at most for only three-quarters of an hour. Often it cannot be induced at all. The animal reacts unusually well to all kinds of sensory stimuli causing reflex muscular contractions, and the spinal vasomotor centers react powerfully to the stimulus of asphyxiation. The effect of shock therefore is past; and yet as a rule one observes no genuine respiration. To maintain the doctrine of the preponderance of spinal respiratory centers under such circumstances, one must assume that these centers react toward shock in quite another way from the other spinal centers.

The fact that hemisection of the spinal cord very often does not result in cessation of the respiratory movements of the same side (Brown-Séquard *et al.*) speaks against the hypothesis of shock. Moreover, when cessation does occur, it is immediately nullified if the phrenic of the opposite side be cut (Porter). If the mechanical injury of sectioning were to produce so strong a shock, as the advocates of the spinal centers assume, hemisection of the spinal cord should stop the respiratory movements on the side of the section for a time at least.

We reach the conclusion therefore that the medulla is not only of great importance in the regulation of respiratory movements, but that it *controls* also the *coördinated activity* of the respiratory muscles. Only in rare cases is such an effect carried out by the nuclei of the spinal cord, and, although we can speak in general terms of spinal respiratory centers, it appears that in comparison with those of the medulla they have but little to do with producing the normal stimuli.

The *exact location* of the respiratory center in the medulla is not yet definitely known. This much appears certain, however, that it is not a small, circumscribed spot, but is a region of relatively large extent. This is what we should expect in view of the very large number of nervous connections which it has.

After median section of the medulla, the respiratory movements of the two halves of the diaphragm (Langendorff) and those of the vocal cords and the nose (Kreidl) continue synchronously—which shows that the influences originating the respiratory movements proceed simultaneously on the two sides of the center. But this synchronism is abolished by section of both vagi, and each half of the body then breathes independently of the other.

That section of the vagus on one side does not always stop the synchronism just mentioned, goes to show that the two centers are connected by commissural fibers. The presence of a crossed connection between the respiratory center and the nuclei of the respiratory muscles follows also from the above-mentioned facts, that respiration can proceed undisturbed on one side after hemisection of the cord on that side and section of the phrenic on the opposite side.

The respiratory movements can be influenced also by stimulation of parts of the brain *anterior to the medulla.* Martin and Booker obtained inspiratory effects by stimulating the surface of a section between the anterior and posterior corpora quadrigemina; Christiani obtained the same on stimulation of the floor of the third ventricle, and expiratory effects on stimulation of the rance of the aqueduct of Sylvius. Finally, the cerebral cortex evidently rcises control over the respiratory movements, as is seen, for example, the extremely fine gradations of these movements which can be executed by a good singer. Respiratory movements can be accelerated or retarded by electrical stimulation of the motor cortex of the dog and cat. The result, according to F. Franck, does not depend upon the place of stimulus, but upon its strength: strong stimulus giving a retardation, weak stimulus an acceleration. The depth of respiration also is changed in one direction or the other.

These parts of the brain act only through the mediation of the respiratory center in the medulla; the fibers running from them to the center are therefore to be regarded as afferent pathways. The warrant for this view lies in the fact already mentioned, that the respiratory movements continue after section above the medulla. Moreover, it is not to be denied that some of the results just discussed can be obtained by stimulation of the conducting pathways. The so-called brain centers for respiration seem therefore to represent only pathways to the center in the medulla. We shall see immediately that these paths and certain parts of the brain are, under certain circumstances, of great service.

§ 3. RESPIRATORY REFLEXES

Like all the other more complicated processes of the body the respiratory movements are influenced by all possible kinds of afferent nerves. But there are two of these paths more important than the rest, namely (1) the vagus, and (2) the fibers which connect the higher parts of the brain with the respiratory center. These accordingly we must consider first.

A. REFLEXES THROUGH THE VAGI

Notwithstanding the voluminous literature that has accumulated on the influence of the afferent vagus fibers, our knowledge of their action on respiration is still very meager. The statements of authors as to the facts bearing on even the most important points differ considerably, and we can therefore present the action of the vagus on respiration only in the broadest outline.

Generally speaking, in the investigation of the influence of any nerve on the processes of the body one obtains the best results by direct stimulation of the nerve. Unfortunately this is not the case with the pulmonary vagus, for section of the nerve is followed by much more profound effects than its stimulation.

A nerve cannot be cut with a pair of scissors without at the same time stimulating it. Besides, an electric current (demarcation current, see page 48) is set up in a cut nerve, and this may possibly exercise a stimulating influence. Gad has shown, however, that the pulmonary vagi can be thrown out of action without stimulation by cooling them sufficiently. For this purpose the vagi are laid upon silver tubes which are filled with a cold mixture (e. g., a solution of ammonium nitrate in water).

Even under such circumstances different authors have not obtained perfectly harmonious results, although all are agreed that after bilateral blocking of the vagus (1) the respiratory frequency falls, (2) that the inspirations become deeper and (3) that the summit of inspiration shows a pause of greater or less length (Fig. 129). But with respect to *expiration* after double vagotomy, views are very divergent: Gad asserts that it no longer reaches its former level, whereas Lindhagen has found that the relaxation of the inspiratory muscles is diminished little or none at all, and Boruttau remarks that sooner or later expiration reaches the same height as before freezing the vagi. According to Gad and Lindhagen, the expiratory pause is nearly always shortened, according to Boruttau it is the same as before or even a little longer. These statements all apply to the rabbit. In the dog, after freezing of the vagi, the expiratory muscles fall into a state of almost regular activity (Boruttau). The breath volume also, according to Gad, becomes smaller after freezing the vagi; according to Lindhagen, it remains on the whole unchanged.

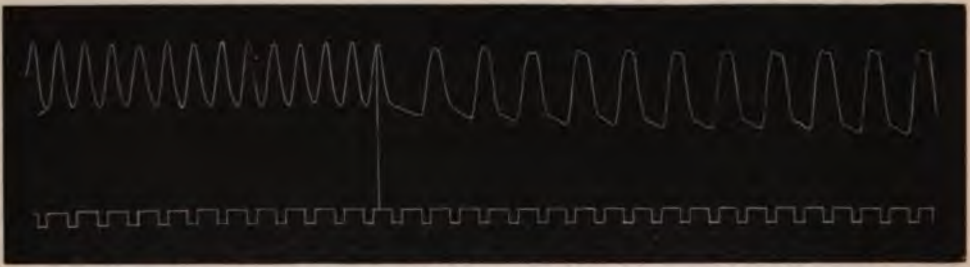

FIG. 129.—The respiratory curve of a rabbit recorded with the apparatus shown in Fig. 122, after Lindhagen. To be read from left to right. The downstroke representing inspiration. The lower tracing is a time record in seconds. At the vertical line the two vagi were "blocked" by freezing.

These discrepancies depend in part at least upon the species of animal used in the experiment, in part upon the depth of narcosis and upon other circumstances not yet fully understood. We shall soon see, however, that they can be explained without great difficulty (cf. page 330).

This much, at all events, is well established by the experiment of disconnecting the vagi by rendering them nonirritable, that the control exercised by those nerves is such as to induce respiratory acts of *greater frequency* and of *less depth* than otherwise, and that the inspiratory pause is thereby prevented. Since this inspiratory pause is not of the least service in the ventilation of the lungs, and the contraction of the muscles of inspiration maintaining it is therefore of no use whatever, it is evident that even when the breath volume before and after disconnection of the vagi is the same, respiration afterwards is carried on with greater effort than normally. The result achieved by the vagus reflex, therefore, is that respiration takes place with *less expenditure of energy*.

The investigations of Hering and Breuer have yielded some very valuable results as to the way in which that regulation is accomplished. Artificial inflation of the lungs inhibits the inspiratory muscles and induces an act of expiration; collapse of the lungs calls out an act of inspiration. *Self-regulation* of the respiratory movements would thus seem to be afforded by the vagi—i. e., when the lungs have expanded to a certain extent inspiration is reflexly interrupted, and when they are afterwards emptied to a certain extent, expiration is interrupted and an act of inspiration is reflexly induced. Both phases of the regulation are lost when the vagi are sectioned.

We may conceive, therefore, that the peripheral endings of the afferent pulmonary fibers of the vagi are excited by the variations in the volume of the lungs, and this is confirmed by the fact that if the vagus be cut on the one side and the lung on the other side be caused to collapse by puncture of the pleural cavity, we get the same result as after section of both vagi (Loewy).

Any more precise explanation of these facts is very difficult to give. It has been supposed that there are two kinds of fibers in the vagus, one of which serves to mediate an inspiratory effort, the other an expiratory effort. But it is also possible to suppose that there is but a single kind of fibers and that the effect produced depends upon the momentary condition of the respiratory center. Thus, if the center already roused to inspiratory action were affected by a stimulus arriving over the vagus, it might be inhibited, and the result of stopping the inspiratory movements might be to inaugurate the relatively passive movements of expiration. Then after expiration proceeds to a certain stage, the collapsing lungs might send up a stimulus by the vagus and the inspiratory phase would be started because the respiratory center at that particular instant was in a condition to discharge such an impulse. We have as a matter of fact some data which can be harmonized very well with this conception of the way in which the respiratory center works (cf. Chapter XXII). But there is still another explanation possible, namely, that the respiratory center constantly tends to discharge inspiratory impulses, but this tendency is inhibited by an impulse resulting from the inflation of the lungs; that after the lungs have collapsed to a certain extent, the inhibition is then removed and the tendency to inspiration once more asserts itself. This explanation is strongly supported by the observation made by Lewandowsky, that inflation of the lungs is accompanied by an action current in the vagus, but that collapse is not.

Artificial stimulation of the central cut end of the vagus ought, one would think, to give a definite answer to this question as to the mode of action of the nerve. But it does not. For in the many experiments of this kind which have been made, both inspiratory and expiratory effects of stimulation have been observed, and the statements of authors differ so much that it is impossible as yet to draw any definite conclusion from them. Still less is it possible to decide from these experiments whether one or two kinds of nerve fibers are concerned.

B. FIBERS FROM ANTERIOR PARTS OF THE BRAIN TO THE MEDULLA

We have already seen that the brain can be sectioned above the medulla without affecting respiration to any considerable extent. If, however, the vagi be sectioned in such an animal, or if the brain be sectioned above the medulla in an animal whose vagi have already been cut, noteworthy alterations of the respiratory movements ensue. Respiration is greatly diminished in frequency, since the inspiratory pauses are now very much prolonged. Inspiration becomes spasmodic, expiration begins very suddenly and not infrequently is aided by contraction of the abdominal muscles. The expiratory pause is of short duration, being soon interrupted by a new, long-drawn inspiration. The breath volume is very much diminished and the animal dies for want of sufficient respiratory exchange in the lungs (Marckwald). These phenomena may appear in varying degree, and it is even stated that the inspiratory spasms may be at times entirely wanting after this operation.

The respiratory center isolated from the higher parts of the brain may therefore maintain respiration in an essentially normal fashion even after section of both vagi, although it is very often unable to do so. At any rate, it appears from these facts that the paths coming from the brain are, under certain circumstances, of very great importance for respiration, and, what is more, that they act in the same way as the vagi nerves—i. e., to inhibit inspiration. Explanation of these phenomena is rendered more difficult because we cannot tell yet to what extent they depend upon the stimulus given at the time the section is made, and to what extent upon the mere disconnection of the pathways.

In view of the *profound influence* of these brain pathways over the movements of respiration, it is not difficult to understand why the severance of the vagi is not always accompanied by the same results; for the effect must depend largely upon the state of excitability of these brain paths at the time. For example, it is possible that the shortening of expiration and the tonic contraction of the inspiratory muscles mentioned by Gad (but not observed by others), was due to a stronger narcosis, on account of which the influence of the pathways in the brain was somewhat weaker than in the investigations of the other authors.

C. OTHER RESPIRATORY REFLEXES

The respiratory movements are influenced in one way or another by *other afferent nerves.* Among these the nerves of the respiratory passages are of the greatest interest, because through them certain reflexes are discharged which are of great service as a means of protection to the lungs.

The nasal openings and the mucous membrane of the nasal passages receive their sensory fibers from the *trigeminal nerve.* Stimulation of this nerve retards respiration. When the mucous membrane of the nose is stimulated at the external openings or on the anterior or posterior end of the middle and lower turbinated bones, or on the corresponding parts of the septum, retardation or expiratory standstill, or even sneezing, results, according to the strength and the kind of stimulus employed. Sneezing may also be abortive —i. e., only the first phase of it, the deep inspiration, may occur. Expiratory standstill may also be induced by stimulation of the skin of the face under certain circumstances, as when an animal's head is submerged in water (Fratschmer).

Inasmuch as these reflexes prevent the entrance of foreign bodies or of noxious vapors into the wider respiratory passages, the afferent nerves of the larynx, particularly the superior laryngeal, *serve to protect* the deeper respiratory passages from foreign bodies. With feeble stimulation of the superior laryngeal slowing of respiration and prolongation of the expiratory pause are obtained; on this account the individual respirations become deeper and longer. With stronger stimulation one may obtain expiratory standstill or active expiratory movements. Inspiratory spasms can be stopped by stimulation of the superior laryngeal.

The *coughing reflex* is discharged principally by the same nerve. The statements of authors do not agree entirely as to the places in the larynx and trachea from which the reflex is produced.

We have the following statements concerning the effect of other afferent nerves. Stimulation of the olfactory by an actual odor either slows or quickens respiration or gives an expiratory pause. Stimulation of the optic by electricity or by light has an accelerating effect on inspiration. The auditory nerve has the same effect. After destruction of the semicircular canals respiration becomes slower and deeper. According to Marckwald, the glossopharyngeal produces respiratory standstill in whichever phase the respiratory center happens to be overtaken by the stimulus, but according to others it behaves just like the other cutaneous nerves. The last named have an inspiratory effect with weak stimulation, and an expiratory effect with strong stimulation. The phrenic also contains afferent fibers which appear to act like the cutaneous nerves, and other afferent muscular nerves behave on the whole like these. With regard to the sympathetic nerves it is stated that the splanchnic causes only an expiratory contraction and that the cervical sympathetic influences both phases of respiration. Finally, by stimulation of the heart and of the aorta, reflex respiratory movements and contractions in the air passages have been obtained.

§ 4. NORMAL STIMULATION OF THE RESPIRATORY CENTER

Seeing then that the respiratory center is reflexly influenced by the most widely different afferent nerves, it would be natural to suppose that it is roused to action only in the reflex manner. But this conclusion is not warranted. We have already seen indeed that the respiratory center isolated from the brain pathways on a vagotomized animal is still very powerfully active. This might be due partly to the stimulating effect of the section and partly to the afferent impulses still reaching the center. But respiratory movements continue when the cerebrum is extirpated, the vagi cut and the spinal cord sectioned below the exit of the respiratory nerves (Rosenthal). It can scarcely be assumed that the respiratory movements are called out by the few afferent impulses remaining after all these operations. Besides there are still other facts which tend to prove that the excitation of the respiratory center is *attributable mainly to the properties of the blood.*

The fœtus in the uterus does not breathe: respiration begins only after birth. What is the cause of the very first act of respiration? The blood of the fœtus is arterialized, so long as the placental circulation is maintained, at the expense of the mother's blood. The temperature of the amniotic fluid in which the fœtus is submerged is exactly the same as that of the fœtus itself, so that it is not subjected to any temperature stimuli nor to any other cutaneous stimuli. At birth the circumstances of life change suddenly: the placental circulation ceases and the skin is subjected to different sensory stimuli. The cause of the first act of respiration is to be sought therefore either in the cessation of the placental circulation or in the sensory stimulation of the skin.

Both these possibilities have their advocates. But from the present information it would seem that the discontinuance of the placental circulation is the real determining factor. It is true that one can produce various motor reflexes, and respiratory movements among them, by means of cutaneous stimuli applied while the placental circulation is still continuous. But such responses are both infrequent and temporary in character. Besides, cutaneous stimulation may be kept up for a long time without ever a sign of a respiratory movement. Contrast with this the result of destroying the placental circulation. However the experiment be performed, whether by clamping or bleeding the umbilical cord, or, the uterus being undisturbed, by poisoning the mother with carbon dioxide or, finally, by bleeding the mother, respiratory movements of the fœtus are always obtained.

If then the first act of respiration be induced by some property of the blood, it follows with a high degree of probability that the *respiratory center is roused to activity in the same way* throughout life. This is confirmed also by a large number of experimental facts. Thus it has been shown that everything that tends to heighten the combustion in the body or to render more difficult the elimination of the gaseous products of decomposition or the absorption of oxygen, produces an augmented respiration. This condition of things is described as *dyspnœa,* if it involves the coöperation of the accessory muscles of respiration.

One might conceive that the products of combustion present in the blood in increased quantity stimulate the end arborizations of the afferent nerves, and that the augmented respiration now under consideration is therefore reflex in nature. Even if this were true, experiment has shown in the clearest possible manner that, in muscular work, for example, the increased respiration is not due to this cause alone; for it appears when the hinder parts of the body, cut off from every possible nervous communication with the fore parts, are stimulated to active contractions, but is entirely wanting if the return flow of blood from the hinder parts is prevented. The blood returning from the posterior active parts has therefore a direct stimulating effect upon the respiratory center (Zuntz and Geppert).

Finally it has been shown that the respiratory movements react very delicately to any change in the carbon-dioxide content of the blood, since, the respiratory frequency remaining almost unchanged, the breath volume of the individual respirations increases with an increasing quantity of CO_2 in the inspired air (Miescher). On the other hand, considerable changes in the oxygen content of the surrounding air (12.5 to 60 volumes per cent) influence the respiration relatively little.

We conclude, therefore, that the respiratory center is excited by the direct effect of the blood or the lymph, but that its action is regulated by all kinds of afferent nerves, especially by the vagi and the brain pathways.

The condition of *apnœa,* or respiratory standstill, which is induced by excessive inflation of the lungs, or in man by one or more very deep inhalations, has often been regarded as a very important fact in support of the conception here presented. Apnœa might have its justification in the unusual opportunity which the blood has, in consequence of unusually ample ventilation, of becoming saturated with oxygen and of freeing itself of carbon dioxide, so that the next respiration would be less necessary. But the matter is not so simple. It has been made clear, for example, that in the rabbit apnœa is much more difficult to obtain if the vagi are cut. These nerves must have something to do, therefore, with bringing about this condition. Moreover, apnœa appears as the result of inflation with hydrogen and can be induced by forcing the same air into the lungs over and over (Gad). Finally, it ceases only after the other organs have shown signs of asphyxiation. We may say, therefore, that apnœa depends at least in part upon an inhibitory action of the vagus upon the respiratory center. But the condition of the blood is not without its importance also, as the following experiment shows. Two dogs were operated upon in such a way that the carotid blood of the first was led into the head of the second. A condition of apnœa was then induced in the second dog by artificial respiration applied to the first (Fredericq). We might distinguish this form of apnœa which is evoked mainly by a diminished quantity of CO_2 in the blood as *true* apnœa, and that mediated by the vagus as *false* apnœa (Miescher).

In *asphyxiation* and *severe hemorrhage* we meet with inhibitory effects upon the respiratory mechanism which are of central origin. Both conditions agree in that the supply of oxygen to the organs of the central nervous system and the CO_2 removed from them are diminished. The consequence is, first a well-marked dyspnœa, upon which follows, after a time, a period of apnœa of greater or less duration. This in its turn is interrupted by a series of new respiratory movements (gaspings). Closer analysis of the apnœa seen here shows that it probably owes its origin to the action of some inhibitory mechanism upon the respiratory center (Landergren).

In certain diseases, in chloral narcosis and certain other forms of poisoning, and with pressure upon the medulla, etc., a special form of respiration is observed, known after two English physicians as the *Cheyne-Stokes respiration.* It consists of a regular rise and fall in the depth of the respiratory acts. No positive explanation of the phenomena has yet been given.

We have spoken so far of the respiratory center as a whole. Closer investigation, however, reveals that here, just as in the mechanism of deglutition, we have to do with *several functional centers bound together,* the anatomical relations of which are at present unknown to us, but the individuality of which can be demonstrated by physiological experiments (Mosso).

It is a fact by this time familiar to us that expansion of the thorax can be accomplished either by the diaphragm or by the rib-lifting muscles. But experiment has shown that in the same individual these two groups of muscles do not always contribute toward the expansion of the thorax in the same ratio. This appears most plainly in sleep, when respiration in man is essentially of a costal type, whereas the diaphragm exhibits a certain paresis, in some persons behaving like an inert membrane. In deep distress just the opposite occurs: the diaphragm moves after the rib movements have ceased. These and other observations to the same effect bear witness that the centers for the rib-lifting muscles and for the diaphragm are to a certain extent independent. Again, the centers which preside over the expiratory muscles are independent; and finally, it has been shown that the respiratory movements of the mouth and nose, as a rule, begin before those of the thorax, which is evidence of the relative independence of the centers for those parts.

THIRD SECTION

THE BLOOD GASES

As long ago as the middle of the seventeenth century, Robert Boyle pumped a gas from the blood, and Mayow (1674) claimed that this gas contained a substance called by him *spiritus nitroœreus* (oxygen). Likewise Priestley demonstrated the presence of oxygen in the blood, and H. Davy found carbon dioxide in it. These statements, however, were disputed by others and only after Magnus (1838) had demonstrated beyond a doubt the presence of oxygen, carbon dioxide and nitrogen in the blood, were the facts generally accepted.

A very important advance in our knowledge of the blood gases was made by the introduction of the Torricelli vacuum for the purpose of extracting them. This method was first used by Ludwig (1859), after Collard, de Martigny, and Hoppe-Seyler had tried it for other purposes. Since that time it has been improved in many ways by many different authors (Fig. 130).

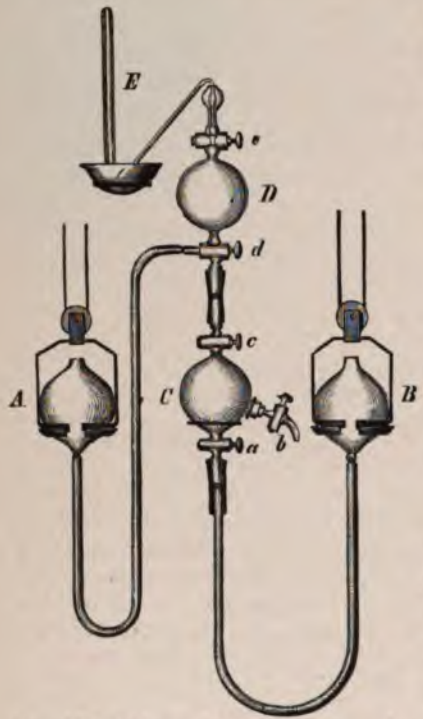

FIG. 130.—Schema of Ludwig's pump for extraction of the blood gases. The pump consists of two bulbs *C* and *D* connected by rubber tubing with the mercury bulbs *A* and *B*. When the stopcocks *a*, *b*, *c*, *d* are opened and the bulb *B* is raised, the bulbs *C* and *D* are filled with mercury. Then if the stopcock *c* is closed and the bulb *B* lowered until the difference in level between *B* and *C* is greater than barometric pressure, a Torricelli vacuum is created in *C*. When *C* is empty of mercury *a* is closed. Then if a vessel containing blood, which has not been exposed to the air, but has been drawn directly from an artery or vein, is connected with *b*, the contained gases will bubble off into *C*. By suitable manipulations, which may be readily understood from the figure, the gases are transferred to *D* and finally to the graduated burette *E*, where they are measured.

§ 1. ABSORPTION OF GASES IN LIQUIDS

When a liquid stands in contact with a space filled with gas, the gas passes from the space into the liquid until the latter has taken up as much gas as the conditions will permit. We must distinguish clearly between two of these conditions.

A. The *liquid exercises no chemical attraction upon the gas.* In this case the amount of gas absorbed depends upon three factors: (1) the nature of the liquid and the gas, (2) the temperature, and (3) the pressure to which the gas is subjected. We may formulate the facts in the following law: The volume of a gas absorbed under different pressures by a given liquid, when reduced to the same pressure and temperature, is proportional to the pressures (Law of Henry).

The *coefficient of absorption* is the volume of the gas (reduced to 0° and 760 mm. Hg.) which is absorbed by a unit volume of the liquid under a pressure of 760 mm.

When several gases within the same space are brought in contact with a liquid, the absorption of each is quite independent of the others, and depends only upon that pressure which the gas itself exerts (Law of Dalton).

This partial pressure of each gas can be calculated, if the total pressure exerted by the mixture and the composition of the mixture are known. It is always that percentage of the total pressure, represented by its volume percentage of the mixture. For example: Water is in contact with air under a pressure of 760 mm. Hg. Air consists of 21 vols. per cent of oxygen, and 79 vols. per cent of nitrogen. The partial pressure of the oxygen therefore is .21 × 760 = 159.6 mm. Hg., and that of nitrogen is .79 × 760 = 600.4 mm. Hg. The absorption of oxygen into water takes place then under a pressure of 159.6 and that of nitrogen under a pressure of 600.4 mm. Hg.

B. *When the liquid exercises a chemical attraction* for the gas, it is not only absorbed physically, but is combined chemically. We have, however, to distinguish two cases, according as the chemical combination does or does not depend upon the partial pressure of the gas. If it does not, the whole quantity of gas will be absorbed whatever the pressure. If it does, that is, if the combination between the liquid and the gas is a function of the gas pressure, the combination will gradually become less and less as the partial pressure diminishes, and with a partial pressure of zero will cease entirely on account of dissociation. In the latter case, therefore, just as when the absorption is purely physical, the quantity of gas entering a liquid is a function of the pressure, but with the important difference that there is here no direct proportion between the volume absorbed and the pressure.

When a liquid has stood for a long time in contact with a certain volume of mixed gases until it has become saturated with the different gases in the mixture, the tension of each gas in the liquid is equal to its partial pressure in the surrounding space. If the partial pressure of any one gas becomes less, the liquid gives off just enough of this gas to establish equilibrium once more, and *vice versa.*

In order to determine the tension of gases in a liquid, the liquid is placed under a definite pressure in contact with a mixture of gases previously analyzed, and, after a certain time, the mixture is again analyzed. The tension of any gas in the liquid is equal to the partial pressure of this gas in the surrounding space, if at the end of the experiment its partial pressure is the same as it was before. In order to hasten the equalization of tensions, the liquid can be shaken up with the mixture of gases, or may be allowed to flow through them in a fine stream.

§ 2. THE BLOOD GASES

A. NITROGEN AND ARGON

These gases are only absorbed physically in the blood. The coefficient of absorption for nitrogen at the temperature of the body is about 0.013–0.02 and the content of nitrogen and argon together is in the neighborhood of 2 vols. per cent; according to Regnard and Schloessing the blood contains some 0.04 vols. per cent of argon.

When the air pressure is very much increased, as in diving and in caisson work, the quantity of nitrogen taken up by the blood must be considerable. If the pressure is removed rapidly, the nitrogen (the other gases of the blood in part also) passes suddenly over into the form of a gas and air emboli are formed in the vascular system, which may cause more or less serious disorders or even death (Hoppe-Seyler, Bert). The gas collected from the heart in such cases consists of about eighty per cent nitrogen.

B. OXYGEN

After Lothar Meyer had demonstrated that the oxygen content of the blood presents but slight variations with different partial pressures, whence it is known to be chemically combined, Hoppe-Seyler showed that oxygen is found *exclusively in the red blood corpuscles* combined with the hæmoglobin.

Many investigations, some of them with hæmoglobin solutions, some with blood, were then made looking to a closer determination of the dependence of oxygen absorption upon its partial pressure. It was not to be expected *a priori* that the hæmoglobin solutions would conduct themselves in exactly the same way as the blood, for hæmoglobin does not occur in the blood corpuscles as such, but in combination probably with lecithin. It appears from these experiments that equal quantities of blood and hæmoglobin combine the same maximum quantities of oxygen, but at lower partial pressures the two behave very differently.

It is impossible to discuss here the facts bearing on the absorption of oxygen by hæmoglobin solutions of different concentrations and the theoretical conclusions appertaining thereto. I shall limit myself therefore to the summarized results obtained by Bohr with dog's blood, by Krogh with horse's blood (Fig. 131), and by Loewy with human blood, all at a temperature of 38°.

Oxygen Absorption in Percentage of Saturation

Partial Pressure of Oxygen; mm. Hg.	Dog's Blood (Bohr).	Horse's Blood (Krogh).	Human Blood (Loewy).
10	33	24	36
20	67	68	53
30	81	82	67
40	..	91	75
50	93	95	81
80	97	98	..

Oxygen in small quantities is present *also in the plasma.* If all the oxygen were to be removed from the plasma at once, dissociation of the oxyhæmoglobin would of course take place immediately, and continue until equilibrium was once more established between the oxygen tension in the plasma and in the blood corpuscles. The coefficient of absorption of oxygen in the blood at body temperature is approximately 0.025.

Since the partial pressure of oxygen in the atmospheric air may be estimated at about 160 mm. Hg., and in the alveoli, as we shall see later, at 120–130 mm. Hg., it follows that under normal circumstances the blood can be saturated with oxygen up to ninety-eight per cent at least (Fig. 131). At a partial pressure of 50 mm. Hg. the absorption of oxygen in man falls to nineteen per cent of saturation, and in the dog to seven per cent. On the other hand, the absorption is not noticeably greater in an atmosphere of pure oxygen.

These conclusions are confirmed by observations on *respiration under different oxygen pressures.* So far as absorption of oxygen is concerned, respiration runs a perfectly even course when the partial pressure of oxygen is raised from twenty-one to sixty, seventy-five, and ninety per cent. There is an increase in the absorption only during the first three minutes of respiration in air rich in oxygen, and this is due to the physical effect of a higher partial pressure in the alveoli. A storage of oxygen in the tissues does no take place under such circumstances (Falloise, Durig).

Neither does the absorption of oxygen suffer any change in consequenc of a fall in the partial pressure to 86 mm. or lower. Only when the atmospheric pressure sinks to 380 mm. (partial pressure of oxygen, 80 mm.) doe a decline in the oxygen content of the blood become evident; at a partia pressure of 55 mm. the decline is marked (Loewy).

The absorption of oxygen becomes less as the carbon-dioxide tension in th blood increases. At an oxygen tension of 50 mm. Hg. and a carbon-dioxid tension of 5 mm., the absorption of oxygen was ninety-three per cent; with th

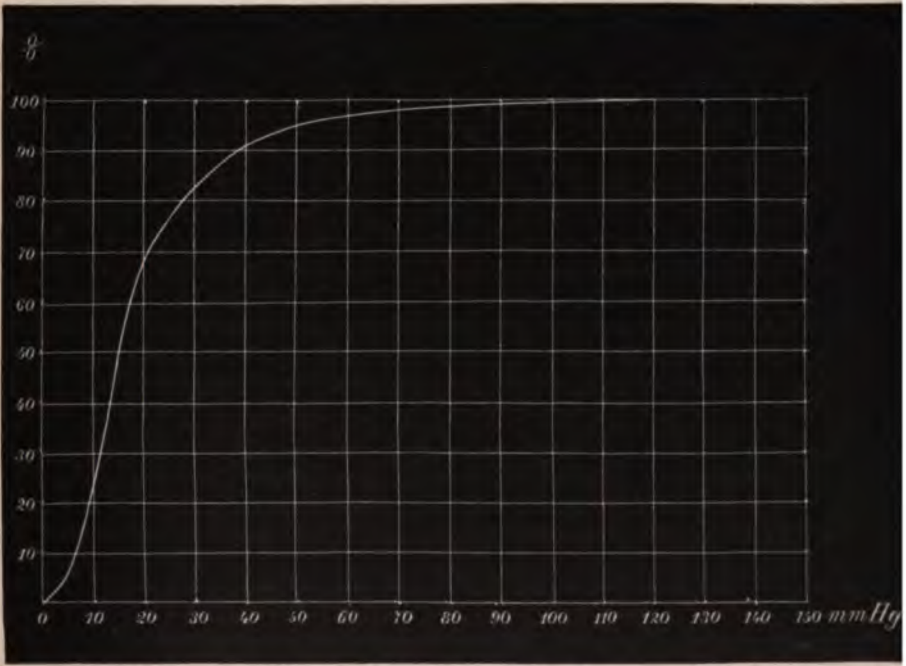

FIG. 131.—The absorption of oxygen by horse's blood, after Krogh. The abscissæ represent th partial pressures of oxygen and the ordinates percentages of saturation.

same oxygen tension and a carbon-dioxide tension of 40 mm. it was seventy eight per cent. As the blood flows through the capillaries the oxygen is gradu ally used up and at the same time the carbon-dioxide tension increases; the lat ter has the effect of conferring a greater tension on the oxygen present, as consequence of which a larger quantity of oxygen can be placed at the disposa of the tissues. The influence of this factor is especially great in asphyxiatio (Bohr, Hasselbach and Krogh).

C. CARBON DIOXIDE

Where carbon dioxide occurs in the blood and how it is combined ar much more complicated questions than in the case of oxygen, and notwith standing many investigations directed to this end, the matter is not to b considered as by any means settled. The difficulty lies just here, that whereas oxygen is evidently present only in hæmoglobin, *carbon dioxide is united with several different substances.*

The researches of Paul Bert, Zuntz, Setchenow, and others have made it perfectly evident that carbon dioxide is present for the most part in *dissociable compounds,* the existence of which depends upon the prevailing partial pressure of CO_2. In accordance with what was said regarding the combination of oxygen with hæmoglobin, it is evident also that a certain quantity of free CO_2 in the blood must be present in physical combination (cf. page 336). The coefficient of absorption of carbon dioxide in water at 37° is 0.569. The dissociable compounds are found both in the plasma and in the corpuscles.

Of the substances in the blood with which carbon dioxide can be combined, sodium bicarbonate $NaHCO_3$ is likely to be thought of first. The phenomena of dissociation in solutions of this salt show however that it cannot play any great part in this connection; for according to Bohr a 0.15-per-cent solution of sodium bicarbonate under a pressure of 0.6 mm. Hg. takes up eighty per cent of the total quantity of carbon dioxide which can be taken up under a pressure of 120 mm., and at a pressure of only 10 mm. it is almost completely saturated.

Again great importance has been ascribed to the phosphates in the combination of CO_2, since it was supposed from analyses of the blood that the plasma contained large quantities of these salts. But it has been shown that the phosphorus found in the ash is primarily a constituent of lecithin and nucleoalbumin, and occurs only in traces as Na_2HPO_4.

The globulin-alkali compounds, on the other hand, appear to be of far greater importance for the combination of CO_2 in the blood. The globulins play the part of weak acids and enter into saltlike combinations with the alkalies of the blood. They can be replaced from these compounds by carbon dioxide and can themselves in turn replace the carbon dioxide.

The significance of this fact will be more apparent from the following:

> If two acids of different avidity represented respectively by a and b be present in a solution of a basic substance, they divide the basic substance between them in the ratio of a/b. Under the influence of equal mass equivalents of the two acids and of the base, $\frac{a}{a+b}$ equivalents of the one acid, and $\frac{b}{a+b}$ of the other will unite with the base. But if the substances are not present in equal mass, the distribution of the base between the two acids will depend upon the relative masses of the two, so that the acid present in the greater quantity relatively, even if its avidity is weaker, will get the greater quantity of the base.

Applied to the problem before us, this would mean that, if the mass of carbon dioxide, or more properly its tension in the plasma, is high, the globulin will be forced out of its alkali compound. If, however, the blood comes into such relations that the carbon dioxide tension falls, the globulins again succeed to their rights and the carbon dioxide leaves the alkali (Torup).

As already observed, carbon dioxide occurs also in the blood corpuscles in the form of dissociable compounds. It is very probable that the globulin-alkali compounds of the blood corpuscles act in the same way as those of the serum. It should be added, however, that the curve of CO_2 absorption for the corpuscles exhibits a much greater dependence upon the partial pressure of CO_2 than that for the serum (Bohr). The constituent most actively concerned here again is the hæmoglobin (Fig. 132).

Hæmoglobin therefore can combine carbon dioxide as well as oxygen. We are not yet clear just how this takes place. Bohr has shown that the absorption of carbon dioxide by hæmoglobin free of alkalies is influenced little or not at all by oxygen. For this reason he assumes that the two gases are combined with different parts of the hæmoglobin molecule—the oxygen with the pigment nucleus, and the carbon dioxide with the proteid component.

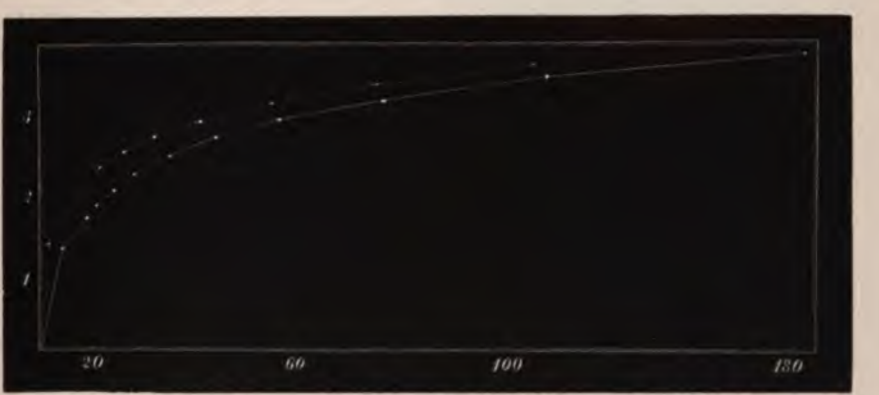

FIG. 132.—The absorption of carbon dioxide in a solution of hæmoglobin, after Bohr, - - - - - - - - 1.76 per cent solution; ———————— 3.8 per cent solution. The abscissæ represent the pressure to which the gas was subjected, the ordinates the amount of carbon dioxide in c.c. absorbed by 1 g. of hæmoglobin.

D. THE QUANTITY OF BLOOD GASES

The *content of gases* is very different in arterial and venous blood. Analyses of the gases in dog's blood, carried out under the direction of Ludwig and Pflüger, give us, according to the summary of Zuntz, the following average percentages: arterial blood, 18.3 vols. per cent oxygen and 38.3 vols. per cent carbon dioxide. By very rapid extraction of the gases Pflüger obtained for arterial blood 22.6 vols. per cent oxygen and 34.3 vols. per cent carbon dioxide. Merely by standing, therefore, the blood uses up oxygen and forms carbon dioxide. From arterial human blood Setchenow obtained 21.6 vols. per cent oxygen and 40.3 vols. per cent carbon dioxide. The percentage of oxygen and carbon dioxide in arterial blood moreover exhibits considerable variations.

The content of gases in venous blood depends naturally upon the *velocity of blood flow* and upon the *activity of metabolism*. That the blood gases exhibit great variations in the different vascular regions, according as the organs are more or less active, is quite beyond question. But at present we have analyses of only the mixed blood from the right heart and from the central veins. These give us, according to the summary of Zuntz, as compared with arterial blood, a mean increase of 9.2 vols. per cent carbon dioxide, and a deficit of 8.15 vols. per cent oxygen, or, after correcting for the venous stasis caused by the catheter, + 8.2 CO_2 and − 7.15 vols. per cent O_2 respectively.

E. THE DISTRIBUTION OF THE BLOOD GASES BETWEEN CORPUSCLES AND PLASMA

The distribution of the blood gases between corpuscles and plasma has been studied by Fredericq on the venous blood of the horse, and in this case only the carbon dioxide was determined; 71.4 vols. per cent were found in the plasma, 49.6 vols. per cent in the corpuscles.

All other determinations along this line relate to defibrinated blood. The following noteworthy facts have been recorded. *Only traces of oxygen* (0.1–0.2 vols. per cent) occur in the serum; almost the entire quantity belongs to the blood corpuscles. We have already remarked that these traces can never be entirely absent from the serum so long as the blood corpuscles contain oxygen at all.

The serum, on the other hand, contains *most of the carbon dioxide.* According to the investigations of Fredericq, Zuntz, and A. Schmidt, the carbon dioxide of the serum amounts to about eighty-six per cent of the total quantity in the blood. However, it is not impossible that by changes taking place in the process of defibrination carbon dioxide might wander from the serum to the blood corpuscles or from these to the serum. The observations of Hamburger indicate that in changing the quantity of gases in the blood, substances pass from the serum to the corpuscles and *vice versa,* and it is possible that such migrations might occur in coagulation, as the result of which the carbon dioxide carriers of the blood would probably become differently distributed between the corpuscles and the serum.

When the whole blood is exposed to a vacuum, the *entire quantity of carbon dioxide escapes.* Not so with the serum: it loses in a vacuum only a part of its carbon dioxide, while a part can be driven out only by the addition of acids. According to Pflüger, the carbon dioxide firmly combined in the serum amounts to five to nine vols. per cent. Since this portion firmly combined is expelled in the presence of the blood corpuscles without the addition of acids, there must be present in the corpuscles certain constituents which act as an acid.

FOURTH SECTION

THE RESPIRATORY EXCHANGE OF GASES

§ 1. MECHANISM OF EXCHANGE BETWEEN BLOOD AND ALVEOLAR AIR

Knowing that the carbon dioxide exists in the blood in the form of a dissociable compound independent of the partial pressure, it is reasonable to suppose that the transfer of carbon dioxide from the blood to the alveoli of the lungs takes place by the equalization of the existing difference in tension.

It is likewise to be assumed that the absorption of oxygen into the blood is the result of a difference in oxygen tension between alveolar air and venous blood.

The method of determining the tension of a gas in a liquid has been given above (page 335). For the measurement of gas tension in the blood, Pflüger let the blood flow in a fine jet directly from the open vessel through a tube charged with a mixture of gases of known composition, and afterwards analyzed the gas. By this method the blood is but a short time in exchange with the mixture of gases, and on this account a complete equalization of tension differences is not insured.

For the purpose of obtaining pure alveolar air for analysis, Pflüger constructed a special instrument, the lung catheter (Fig. 133). This consists of two tubes, one inclosed within the other. The outer tube, made of hard rubber, communicates with a soft rubber bulb (*a*), the thin-walled end of which can be inflated by means of the air pump (*b*) after it is introduced into the bronchus, so as to close hermetically the bronchial opening. The inner tube (*d*), an ordinary elastic catheter, places the confined lung space in connection with a suitable tube (*c*) filled with mercury. After the air has been confined for the desired length of time, it can be drawn into this tube *c* by allowing the mercury to run out.

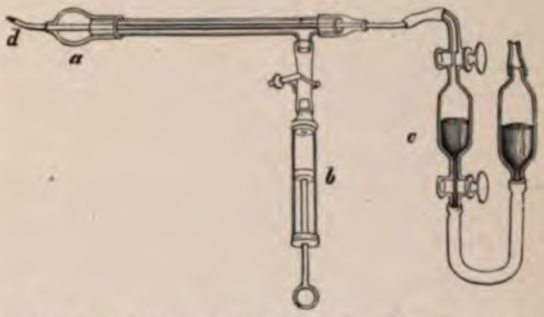

FIG. 133.—The lung catheter, Ludwig's construction.

From determinations carried out by this method, chiefly in Pflüger's laboratory, the tension of carbon dioxide in the arterial blood has been found to be 2.8 atmospheres, and in the venous blood 3.8 to 5.4 atmospheres; that of oxygen in the arterial blood at most fifteen per cent of one atmosphere. Since the partial pressure of carbon dioxide in the alveolar air proved to be less, and that of oxygen greater, than the tensions of these gases in the arterial blood, evidence was found for the conception that the respiratory exchange takes place by a *simple equalization of tensions*.

Bohr has entered the lists decidedly opposed to this view. By a special method he determined the tension of the gases in flowing blood, and analyzed the expired air at the same time. He found that the tension of carbon dioxide in the arterial blood may be lower than the partial pressure of carbon dioxide in the air which passes the bifurcation of the trachea; also that the tension of oxygen in the arterial blood may be greater than the partial pressure of oxygen in the same air. Other factors than the tension differences therefore must be concerned in the respiratory exchange. Bohr lays special stress upon the activity of the alveolar wall, which is said to *secrete carbon dioxide* and actively absorb oxygen.

In general it may be assumed that the total amount of carbon dioxide given off in the lungs comes to the lesser circulation from the veins of the greater circulation. However, the opinion was long ago expressed by Lavoisier in his studies on the respiration, that carbon dioxide is formed in the lungs; and recently Bohr and Henrique have published experiments which purport to show that a considerable part (two to sixty-six per cent) of the carbon dioxide given off is formed there. If these results should be confirmed, it would be necessary to suppose that in the combustions going on in the body in addition to carbon dioxide, a number of intermediary products of decomposition are formed, given off to the blood, and there further oxidized (cf. page 339); also, possibly, that some final oxidation takes place in the lungs.

§ 2. EXCHANGE OF GASES BETWEEN BLOOD AND LYMPH

During its passage through the capillaries the blood gives off oxygen to the tissues and receives carbon dioxide from them. We know very little at present about the manner of this exchange in the tissues. But, since the tension of oxygen in the tissues is extremely small, while according to Strasburg the tension of carbon dioxide there exceeds that of the venous blood (CO_2 tension in venous blood 42 mm. Hg., in the intestine 59, in the bile 51, in acid urine 67), the exchange might be looked upon as a simple matter of equalizing the tension. In view of the facts with which we have just become acquainted under respiratory exchange in the lungs, and since the consumption of oxygen (cf. page 27) does not depend upon the oxygen tension but upon the activity of the tissues, it is possible that the vital activity of the vascular wall should exercise some influence—but we have no positive information on this at present.

§ 3. CHANGES PRODUCED IN THE RESPIRED AIR

The excretory products eliminated in the breath are carbon dioxide, water vapor and possibly some other gaseous substances as yet imperfectly known.

Inspired air contains in round numbers twenty-one vols. per cent oxygen and seventy-nine vols. per cent nitrogen, if we disregard argon, etc. To these are to be added some carbon dioxide, which amounts to only 0.03 per cent in atmospheric air, but sometimes to considerably more in room air, and water vapor, the quantity of which varies within wide limits.

The *expired air is saturated with water vapor,* which for the most part has its source in the respiratory passages (cf. page 323). To what extent this water vapor represents a product of metabolism cannot yet be decided.

In different animals and in different individuals, as well as in the same individual under different circumstances, the *amount of carbon dioxide* in the expired air exhibits wide variations according to the depth and frequency of the respiratory movements, etc. The figure generally given for the normal percentage of CO_2 in the expired air of man is 4.1 vols. per cent (Vierordt). With quicker and deeper respirations the lungs are better ventilated and the amount of CO_2 sinks to about 2.5–2.78 vols. per cent. Along with this the quantity of CO_2 given off per minute becomes greater, which in itself however serves only as an expression of the improved ventilation and signifies nothing concerning the way in which the formation and elimination of CO_2

are influenced by the altered frequency and extent of the respiratory movements. As far as this latter question is concerned, numerous observations teach us that augmented respiration increases the absolute output of CO_2—not in consequence of the greater exchange of air, but *on account of the increased* work of the respiratory muscles.

The *percentage of oxygen* in the expired air is of course less than that of the inspired air, and in fact it decreases more as a rule than the percentage of CO_2 increases. When carbon burns in oxygen, the volume of the gas does not change. Since in respiration, however, the amount of oxygen which has disappeared is greater than that of the carbon dioxide formed, it follows that the oxygen is used in the body for other oxidations than that of carbon. The ratio between carbon dioxide formed and oxygen used $\frac{CO_2}{O_2}$ is called the *respiratory quotient.*

The *value of the respiratory quotient* is very different under different circumstances, and depends upon the kind of foodstuffs which at the time are being burned in the body. The carbohydrates contain in their molecule just as much oxygen as is necessary to completely utilize their hydrogen. The total quantity of the inspired oxygen therefore can be used for the oxidation of their carbon. Hence, if carbohydrates exclusively are being burned, the value of the respiratory quotient will be 1.

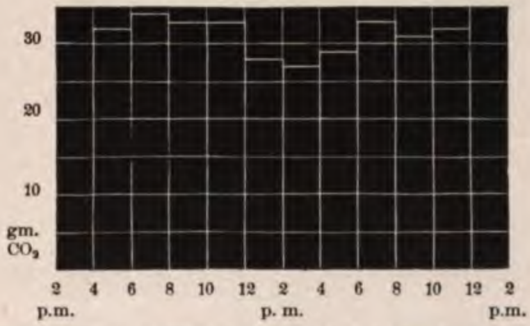

FIG. 134.—The amount of carbon dioxide measured in two-hour periods, expired by a woman who slept during the entire time, and who for five days previously had eaten scarcely anything.

Fat and proteid require more oxygen than carbohydrates for their complete oxidation because the oxygen contained in their molecule is not sufficient for the complete saturation of their hydrogen. Consequently when these substances are being burned the respiratory quotient will be less than 1—for fats 0.71 and for proteid 0.78. (Fat contains on the average 76.5 per cent C, 12 per cent H, 11.5 per cent O; proteid (dry muscle) 50.5 per cent C, 7.6 per cent H, 15.4 per cent N and 20.97 per cent O, of which 11.3 per cent C, 2.8 per cent H, 15.4 per cent N, and 11.44 per cent O are eliminated in the urine and fæces, leaving 39.2 per cent C, 4.8 per cent H, and 9.53 per cent O to be eliminated in the breath.) Since it only rarely happens that carbohydrates alone are burned in the body, the respiratory quotient as a rule is less than 1, and with ordinary food may be estimated at about 0.8. When fat is being formed from carbohydrates and being stored the respiratory quotient may exceed 1.

Reduced to dryness and to 0° the expired air, therefore, has a smaller volume than the inspired air. Measured directly its volume is greater because of its water vapor and higher temperature.

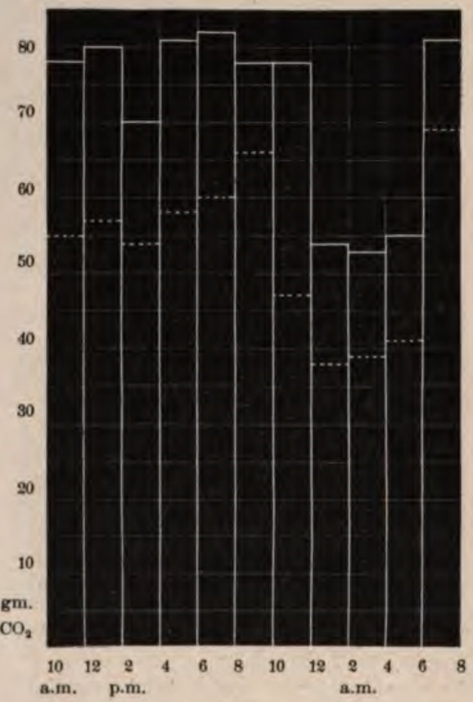

FIG. 135.—The elimination of carbon dioxide: ———— on ordinary diet (mean for three days); and - - - - - - - - - while fasting (mean for five days). All the determinations were made on the same individual, a man twenty-five years old. On the food days he slept between 12 o'clock midnight and 6 A.M. On the fasting days he slept between 10 P.M. and 6 A.M.

For example, let us suppose that the inspired air (500 c.c.) has a temperature of 20° C., and that it is saturated with water vapor at this temperature (tension 17.4 mm. Hg.). Expired air, we will suppose, has a temperature of 37.5° C., is saturated with water vapor (tension at this temperature 47 mm. Hg.) has lost 4.783 per cent oxygen and has gained 4.380 per cent carbon dioxide. Measured directly then the expired air would have a volume of 554.89 c.c.—i. e., approximately one-ninth greater than inspired air. The difference would evidently be greater the colder the inspired air (J. R. Ewald).

During recent years the question whether the expired air contains poisonous gaseous constituents has been very actively discussed. Brown-Séquard and D'Arsonval on the basis of numerous experiments had answered the question in the affirmative. Their statements were put to the test by several other authors, but by most of them without results. Formánek, however, proved by exact methods that the poisonous effects observed by the above-named authors on confined animals came in fact only from ammonia set free from the solid and fluid excretions of the animal employed.

Since the carbon dioxide in the air may rise to four or five per cent and higher without exercising any harmful effects, we may conclude that the indisposition which results from long confinement in badly ventilated or overcrowded rooms is due, not to the influence of any poisonous constituents of the expired air, but to other circumstances—e. g., higher temperature, higher humidity, gaseous substances coming from the intestine or from an unclean skin, etc. It is assumed of course that the ventilation is not so bad that carbon dioxide accumulates in too large quantities.

§ 4. THE ABSOLUTE AMOUNT OF RESPIRATORY EXCHANGE

In the section on the nutrition of man (page 137) will be found fuller information bearing on this subject. Here we must limit the discussion to some facts concerning the *variations in the normal output* of carbon dioxide (Figs. 134, 135, and 136) estimated for two-hour periods.

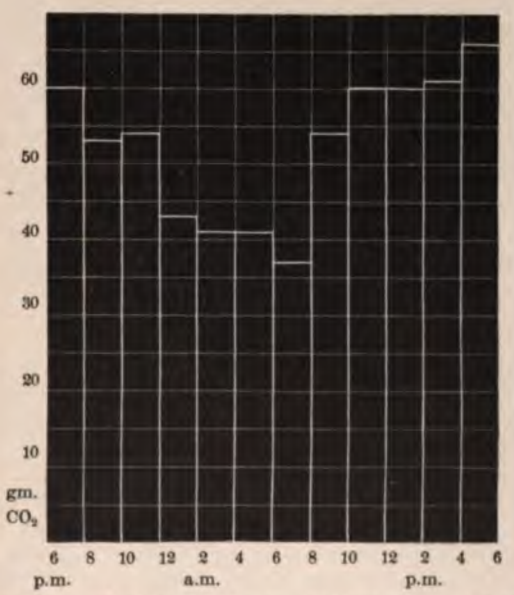

FIG. 136.—The elimination of carbon dioxide, in two-hour periods, by an eleven-year-old boy. He slept between 10:30 P.M. and 8 A.M.

In view of the many circumstances which affect the amount of metabolism and therefore the *output of CO_2*, it is impossible to specify in a few figures the quantities excreted daily. In a man not at work it can be estimated on the basis of direct observations for twenty-four-hour periods at 0.5 g. per hour per kilogram of body weight, which for a person of the average weight of 70 kg. would amount to 35 g. per hour and 840 g., or 427 l. per twenty-four hours. At heavy physical labor the hourly output of CO_2 may rise to 169 g. and higher; in complete bodily rest it falls to about 20 g. per hour (Fig. 134).

The *intake of oxygen,* like the output of carbon dioxide depends upon the food, work, temperature, age, etc. With a respiratory quotient of 0.80 the oxygen consumption corresponding to a carbon dioxide output of 427 l. per day would be 534 l., or 764 g. According to the indirect determinations of Pettenkofer and Voit, in the grown man fasting and at rest it amounts to 740–780 g., fasting and at work 1,070 g., on a moderate diet and at rest 700–900 g., on a moderate diet and at work 1,000 g., etc. By direct determinations with the respiration apparatus of Hoppe-Seyler the oxygen absorption in a grown man on a mixed diet and not at work amounted to 559–586 g. per twenty-four hours (Laves). In experiments of shorter duration Magnus-Levy found the oxygen absorption in a fasting individual at complete rest to be 17.5–19 g. per hour, which corresponds to a daily absorption of 428 to 456 g.

CHAPTER X

THE LYMPH AND ITS MOVEMENTS

The lymph or "tissue fluid" is the medium in which the cells of the body live. In part it is imbibed into the living substance itself, and in part is collected in otherwise empty spaces about and between the cells. The entire body is permeated throughout with such spaces which are of the greatest variety of forms: clefts, minute canals, sheaths, sacs, etc., and exhibit the greatest possible difference in size. Some, such as the so-called serous sacs, like the peritoneum, the pleura, the pericardium, the serous sacs surrounding the organs of the central nervous system, etc., are enormously large, while others can only be detected with high magnification. All these fluid-filled spaces, of whatever kind, communicate[1] with the lymph vessels, and through them with the blood system.

The lymph comes from the blood and is conveyed again by the lymph vessels to the blood. Besides, certain constituents of the lymph are taken up directly into the blood vessels through the permeable walls of the capillaries.

From the blood the lymph receives all the substances necessary for the life of the cells; from the cells it receives the products formed in their own life processes, both those which arise as a result of the dissimilatory activities and those which are formed by synthetic processes in one organ or another for use in still other organs. It follows that the lymph in the different organs *must be of different composition*, since on the one hand the requirements of the different organs are different both qualitatively and quantitatively, and on the other the products of assimilation and dissimilation are different.

However, we have at present no complete analyses of the lymph in the different organs, nor of the lymph flowing from the different organs; our knowledge is limited almost entirely to the composition of the mixed lymph to be obtained from the thoracic duct.

§ 1. THE CHEMICAL PROPERTIES OF THE LYMPH

The lymph, as one of the discoverers of the lymph system (Olaus Rudbeck, 1673) remarked, *is a water-clear liquid of salty taste, which coagulates spontaneously.* Our knowledge is at this time but little more extensive.

The lymph contains scattered leucocytes. Its chemical composition agrees qualitatively with that of the blood plasma but quantitatively differs from it chiefly in that the lymph is poorer in proteid. In comparison with the total proteid of the plasma, the lymph is said to contain less globulin.

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[1] According to the recent researches of McCallum and Sabin, the lymph vessels are closed tubes like the capillaries. If so, we must think of the tissue-spaces and serous cavities as separated by thin walls from the real lymph channels.—Ed.

In the dog's lymph Hammersten found almost no oxygen, but found thirty-seven to fifty-three vols. per cent of carbon dioxide. It is stated that the carbon dioxide tension in the lymph is greater than in the arterial blood, but less than in the venous blood.

According to analyses at present available, the lymph of man contains: 93.5–95.9 per cent water, 4.2–6.4 per cent solids, 0.04–0.05 per cent fibrin, 3.5–4.3 per cent proteid, 0.7–0.8 per cent ash, 0.4–0.9 per cent fat, cholesterin and lecithin.

There are found in lymph also substances which have a *marked influence on certain parts of the central nervous system.* If lymph from the cervical lymph trunks of the dog be injected into the internal carotid of the same animal, changes in the circulation are noted. Certain nervous mechanisms are stimulated, others are paralyzed, and the form of the blood-pressure curve is altered. Similar injections of blood have no such effect (Asher and Barbèra). The chemical nature of these substances is not yet perfectly known, but in all probability they are products of combustion in the organs.

The *quantity of lymph,* inclusive of the chyle, which flows through the thoracic duct into the blood stream in twenty-four hours may be estimated for man at one to two liters. In view of the passage of certain constituents into the blood by way of the capillaries, an exact determination of the quantity of fluid flowing through the thoracic duct possesses no great interest.

§ 2. MOVEMENTS OF THE LYMPH

To determine the flow of lymph quantitatively, a fistula is made in the thoracic duct or in one of the larger lymphatics. The quantity which flows from the thoracic duct immediately after the operation is fairly large owing to the stoppage incident to tying-in the cannula, but it declines rapidly. In the further course of an experiment of this kind the quantity may either remain constant for a time, or may continue to fall; the latter appears to be the rule.

No lymph at all is to be obtained from the main lymph vessel of an extremity, unless its flow is aided by active or passive movements of the part. From this we may conclude that by far the greater part of the lymph flowing from the thoracic duct, when the animal is perfectly quiet, comes from the viscera.

The lymph vessels are always full; the pressure of lymph in the cervical trunk of the dog and horse is from 10 to 20 mm. soda solution. The *velocity* of lymph flow is much less than the velocity of blood flow in vessels of similar size.

Among the forces which maintain the flow of lymph, the tension which is exerted by the *elasticity of the tissues* should be ranked first; every increase of tissue fluid must naturally heighten this tension and thus accelerate the flow of lymph. The movements of the individual parts of the body whether they be passive or active, occasion elevations of pressure on the lymph spaces and lymph vessels, which act in the same way as the tension of the tissues to favor the flow. Besides, throughout such passive tissues as tendons and fascia stresses occur, in some cases regularly and rhythmically as the result of voluntary movements, but more often quite accidentally, which favor the movements of the lymph.

In certain animals (rats and guinea pigs), the walls of the lymph vessels execute *rhythmical contractions*, and in the Amphibia the flow of lymph is aided materially by the so-called *lymph hearts*—small contractile structures situated on both sides of the coccyx and beneath the scapula. The lymph is forced by their contractions into the iliac and jugular veins respectively.

The liquid flowing from the villi of the intestine through the lacteals is forced along by contraction of the smooth muscle fibers of the villi. Finally, the *suction of the thorax* must be taken into account, inasmuch as it affects the flow of the lymph just as it does the flow of blood in the central veins. It is evident at once that the *valves of the lymph vessels* are of great importance for all of the above-named factors.

The smooth muscles of the *receptaculum chyli* and of the thoracic duct at least are under the influence of the central nervous system. The left splanchnic contains dilating fibers, and, though in smaller numbers, constrictors also, for the *receptaculum*. The motor nerves for the thoracic duct are in the thoracic sympathetic. Here also the dilator fibers are superior to the constrictors in their control over the wall of the duct. The dilating nerves can be excited reflexly by various afferent nerves (Gley and Camus).

§ 3. THE FORMATION OF LYMPH

Since the blood pressure in the capillaries is higher than the tension of lymph in the surrounding tissues, it was for a long time supposed that the lymph is *pressed out* of the capillaries by this difference in pressure (filtration), and that the *osmotic processes* between the blood and lymph exercise a more or less considerable influence on both the quantity and composition of the latter.

The most important experimental support of this view was the easily confirmed fact that the lymph streams become swollen considerably after tying off a vein, as a consequence of which the pressure in the capillaries is increased (venous hyperæmia). On the other hand it was shown that an increase in capillary pressure produced by dilatation of an artery (arterial hyperæmia) often does not increase the formation of lymph in the least.

If the cervical and brachial nerves of an animal be cut so that the vessels of the arm are removed from the influence of the nervous system, and the cervical spinal cord be then stimulated, the blood vessels all over the body, with the exception only of the arm, contract, wherefore the blood flow to the arm, and consequently the blood pressure in its capillaries are greatly increased. Notwithstanding this, the quantity of lymph flowing from the lymph vessels of the arm by the aid of passive movements is not increased in the least, but continues to fall gradually as before (Ludwig and Paschutin). The same is true of the submaxillary gland, when after section of the cervical sympathetic of an animal poisoned with atropine, the spinal cord and the chorda tympani are stimulated: the greatly augmented supply of blood to the gland produces not a trace of œdema (Heidenhain).

The difference in pressure between the blood and lymph, therefore, is at least *not the only cause* of the formation of lymph.

After the insufficiency of the filtration hypothesis had been established, there still remained a possibility of explaining the formation of lymph by reference to osmotic processes. In the numerous investigations which have been carried on in the last few years many facts have been observed which present no special difficulty for this hypothesis. But there are other phenomena which cannot be explained so simply, and which have led therefore to the hypothesis that not only the difference in pressure and the osmotic processes, but *some specific secretory process* in the capillary wall also is concerned in the formation of lymph (Heidenhain).

Of the facts which led Heidenhain to adopt this view, some have lost much of their force, in view of more recent work; others, however, are not yet satisfactorily explained from the physical point of view. We shall discuss briefly and in order the most important of these phenomena.

1. If a hypertonic solution of common salt or of sugar be injected into the blood vessels, within a short time a large quantity of water passes from the lymph into the blood, while simultaneously the salt or sugar rapidly disappears from the blood, and the lymph stream becomes greatly augmented for a long time.

This phenomenon might be explained by saying that the vascular wall is less permeable for sugar (or salt) than for water; consequently water passes into the blood vessels by osmosis until the sugar can pass out. Once out of the vessels the sugar in its turn draws water from the tissues and thus occasions the increase of lymph. Among the difficulties which such an explanation encounters is this, that, according to Heidenhain, the content of sugar in the lymph surpasses that found at the same time in the whole blood or in the serum: the escape of sugar from the blood, therefore, cannot be explained by any process of osmosis, but may be due to the activity of the capillary wall.

Cohnstein, in opposition to this view, remarks that it is not fair, because of the slow movement of lymph, to compare the composition of blood and lymph drawn at the same time, but in order to obtain harmonious results one must compare only the maximum concentrations of the two. If this rule be observed, the maximum concentration of serum is generally higher than that of the lymph. But sometimes the opposite relationship obtains, and this Cohnstein thinks may be because the blood test is not made immediately after injection of the fluid. But, again, it might be said that the injected fluid had not had time to mix thoroughly with the blood. Be that as it may, the phenomena now under discussion can undoubtedly be explained on a purely physico-chemical basis, and constitute therefore no conclusive proof for the secretion hypothesis.

2. Likewise, the fact emphasized by Hamburger that the osmotic tension of the lymph flowing from the lymphatics of the extremities under perfectly normal circumstances is greater than that of the blood from the corresponding arteries, is not a co [illegible] f for it is conceivable that the lymph owes its high tension t [illegible] ects of decomposition from the tissues (Koranyi).

[illegible] ar to be of greater weight. There is a large number [illegible] which when injected into the blood produce a [illegible] n of lymph (Heidenhain). To these belong curare, extracts of crab's muscle, leech extract, dilute solutions of egg albumin and peptone, nuclein and metabolic products of Bacteria, water extract of strawberries, etc. The seat of this increased formation is almost exclusively in the liver and the pressure in the liver capillaries shows only a temporary rise. The cause in this case cannot be sought in any sort of filtration, and the osmotic processes cannot play any part, since the quantity of injected substance was always very small. It is most natural therefore to conceive of the process as secretory in nature, unless one supposes with Starling that the liver capillaries are injured by the substances used and thus permit a freer passage of fluid—which however is not yet proved.

The flow of lymph from the glandular organs at least always increases when the glands are active. Stimulation of the salivary glands through their secretory nerves for example raises the quantity of lymph in the vessels of the neck. Injection of sodium taurocholate produces a copious secretion of bile and the lymph stream in the lymphatics of the liver swells in size. The same is true when the formation of urea in the liver is intensified by the injection of ammonium tartrate; and we should probably include here also the increase in the quantity of lymph flowing through the thoracic duct during digestion of proteid.

According to Asher and Barbèra, the activity of the gland cells is the primary phenomenon in these processes and the increased production of lymph is only secondary. It is clear of course that a secreting gland must receive more water, the more active is its production. It can be easily understood also that a certain part of this water should be carried away by the lymphatics; the only question is, What are the forces which cause the increased output of lymph?

Here, again, one may conceive of an active participation of the capillary endothelium, and yet the possibility of a change in the osmotic tension of the lymph by the process of secretion of such a nature that new quantities of lymph would pass out of the capillaries by pure osmosis is not excluded. A definite decision between these two explanations is not possible at present, because exact quantitative determinations of the osmotic pressure of the lymph and of its changes during secretion are wanting.

4. Not only water, however, but salts and organic foodstuffs also pass from the blood into the lymph. Here again theoretical explanation of the phenomena meets with certain difficulties. The metabolism of the different organs of the body differs greatly with respect both to quantity and kind; they require different substances in very different quantities. A milking cow, for example, secretes daily from the milk glands 25 l. of milk containing 42.5 g. of calcium; which means that from the capillaries of the milk glands there passes a much larger quantity of calcium than from all the other capillary regions of the body put together.

This holds true with regard to combinations of iodine by the thyroid gland. The thyroid takes up the iodine occurring only in excessively small quantities throughout the body (the blood of the dog contains according to Gley and Bourcet 0.01–0.11 mg. of iodine per liter) and stores it up in a compound very rich in iodine (Baumann).

The different organs, therefore, must possess a *specific power of selection*, in virtue of which each levies upon the blood for the constituents necessary to its activity. Since however the gland cells are not attached to the capillary cells, but are separated from them by lymph spaces, they cannot themselves exercise this power of choice but must delegate it to the capillary cells.

Cohnstein rejoins with the supposition that after the parenchyma cells of the glands, etc., have removed a certain constituent from the lymph, the latter receives its replenishment from the blood by a process of diffusion, so that no delegation of the selective power is necessary. But to make this supposition valid, it must first be shown that the distribution of the individual substances in the lymph of the different organs is the same, that, for example, iodine occurs in the lymph of all the organs as plentifully as it does in that of the thyroid gland. Only when such proof has been furnished can we regard the assumption of an active participation of the capillary wall in the delivery of these substances as finally refuted.

5. We can say nothing definite at present concerning the entrance of proteid and fat into the lymph. What we know of filtration elsewhere, in the opinion of the author, speaks very decisively against the assumption often made, that we are here dealing with a simple physical process of this kind.

To sum up the foregoing discussion we may say, that *purely physical forces* such as difference of pressure and of osmotic tension *are not of themselves sufficient* to explain all the phenomena incident to the formation of lymph. At present we are forced to suppose that the *living capillary wall participates* in the formation by some sort of a secretory process. This does not exclude the purely physical factors, although we cannot as yet distinguish what part should be ascribed to them, and what to the vital activity of the capillary wall.

If this view be correct, it follows that the capillary wall[1] can be thrown into action by the most different substances, including such as are present in the normal composition of the blood; also that the capillaries in the different organs are different in certain respects. In general they offer a certain resistance to the passage of water and other substances, but after death or under certain abnormal conditions—e. g., venous stasis, poisoning with chloroform, chloral, and ether (Magnus)—this resistance is more or less reduced. Hamburger seems even to assume that the increased outflow of liquid in venous stasis is caused by the stimulating action of lymphagogic substances collected in larger quantity. The following phenomenon observed by Hamburger may be mentioned in this connection. If a horse with his head perfectly quiet moves his legs, the flow of lymph in the cervical lymphatic trunk increases. We probably have to do here with an excitation of the vascular wall induced by some product formed in the working muscles and given off to the blood.

Against the general view which is given most prominence here it might be objected that the capillary wall is so thin that it is bound to permit a plentiful filtration, and that this physical process must therefore play a much greater part than has here been assumed. It appears, however, that other living animal membranes, if they are uninjured, do not permit any filtration. This is the case, for example, with the lung of the frog, and with the membrane of Descemet (Leber) in the eye. When they have been killed they filter very well; but in the living state they do not let a single drop of an indifferent liquid pass through. The thinness of the capillary cells signifies nothing against the assumption that they can develop a powerful secretory activity. They are thin because they live immediately in the blood and hence need not maintain a reserve store of material within their own borders.

§ 4. THE LYMPH GLANDS

Our information as to the functions of the lymph glands is at present very meager. From what we know of the leucocytes on other grounds it is conceivable that the glands change the substances in the liquid flowing through them in some way. From the fact that they swell up under various pathological conditions we may also conclude that they retain injurious substances to some extent and thus prevent their entrance into the blood stream.

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[1] And possibly the wall of the lymphatic vessels; see note page 347.—Ed.

If the afferent and efferent vessels of a lymph gland be tied, but the blood vessels be left open, the leucocytes in the gland disappear (Koeppe). From this it would seem to follow that the lymph constitutes a stimulus for the lymph gland, to which the latter responds by the formation of leucocytes (Asher and Barbèra).

§ 5. ABSORPTION FROM SEROUS CAVITIES

Dissolved substances as well as water can pass from the lymph into the blood vessels. This we know because solutions injected subcutaneously or injected without injury into the blood vessels of a limb which is connected with the rest of the body only by means of the blood vessels, are completely absorbed (Magendie).

Substances can also be absorbed from the serous cavities of the body, such as the peritoneal space, the pericardial cavity, pleural cavity, etc. A fluid, whether serous in character or not, and whatever its origin, when injected into such a cavity is always first rendered isotonic with the blood plasma. If it be hypertonic—as e. g. a two-per-cent solution of NaCl—to begin with, it is diluted by the addition of water until it has exactly the osmotic pressure of the blood plasma; if it be hypotonic—e. g., a 0.5-per-cent solution of NaCl—it loses water until it has the osmotic tension of a 0.92-per-cent NaCl solution, and then in either case remains at this concentration until absorption is complete.

These alterations of the osmotic pressure are unquestionably to be referred to osmotic processes going on between the injected fluid and the blood plasma.

It might be very naturally supposed that absorption from these cavities takes place through the lymph spaces which open into them, and in the case of the pleural cavities and the peritoneal space this seems to be quite readily demonstrable. But absorption from the abdomen and the thorax can take place also through the blood vessels, and in fact the latter seem to play the chief rôle here.

Now, since the blood vessels can, as may be assumed without definite proof, absorb fluids isotonic with their contents, one would be inclined at once to ascribe the action to some specific vital activity of the endothelial cells. But the surprising thing is that absorption from these cavities can take place to about the same degree in dead animals as in live ones. Active cells therefore are not essential to the process.

There remains to be mentioned, besides the processes of diffusion and the attractive power of proteid for water (cf. page 154), the process of imbibition. All tissues, living as well as dead, have the power of taking up fluids either by molecular imbibition—i. e., of absorbing fluids through homogeneous substance —or by capillary imbibition—i. e., through discrete pores. Hamburger supposes that by imbibition of the first kind fluids are absorbed by the homogeneous cement substance between the endothelial cells lining the peritoneum, and that by the same process the fluid is passed on into the subepithelial connective tissue. Also, that the cement substance between the endothelial cells of the capillaries acts in the same way, and by means of the minute lumina of the capillaries an imbibition by capillarity assists in draining the abdominal cavity.

This power of imbibition, however, is limited and would soon come to a stop, since a given volume of tissue could only take up a certain quantity of fluid.

After a time a plethoric state would be reached which would cause stagnation unless the fluid entering the capillaries were rapidly drained off in the blood stream. In fact it is found that perfusion of fresh serum through the blood vessels of a dead animal accelerates the process of absorption very materially.

Besides we are not to suppose that the mechanisms here spoken of are everywhere the means of absorption of fluids by membranes, for it is fairly certain that in the absorption of substances by the frog's skin the epidermal cells take up the substance from the outside and pass it over into the inside. A surviving frog's skin placed between solutions of NaCl of equal strength will take up salt from the outside surface and pass it through to the inside surface—a thing which does not occur in the dead skin. Similar phenomena have also been mentioned in connection with the absorption from the intestine of mammals (page 301).

Solid particles also like milk droplets, carmine granules, etc., can be absorbed from the serous cavities probably by way of the lymph spaces. They can also be ingested and carried away by leucocytes.

Our conclusion must be that, aside from the passage of fluids into the open channels [if such there be; cf. note page 347] communicating with the serous cavities, the purely physicochemical processes of diffusion, chemical attraction, molecular and capillary imbibition go far toward explaining the absorption of liquids from those cavities.

REFERENCES.—*Alexander Ellinger*, "Die Bildung der Lymph" in "Die Ergebnisse der Physiologie," I, 1, 1902.

CHAPTER XI

THE INFLUENCE OF THE ORGANS ON ONE ANOTHER

ALTHOUGH the individual organs, and indeed the individual cells of the Metazoa, carry on their life to a certain extent independently, they are in many ways dependent on one another. In truth it is only by this mutual relationship that the activity of the numberless minute parts can result in the life of the whole body.

This interdependence of the individual parts of the body is made effective primarily through the nervous system. There occur, however, between the separate organs many reciprocal influences more or less independent of the nervous system, which are of very great importance for the functions of the body and which participate largely in the regulation of its mechanisms. Here belong osmotic processes brought about by alterations in the cells or in the lymph, and the influence which different organs exercise on one another by means of products formed in them and delivered to the liquids of the body.

§ 1. THE OSMOTIC PHENOMENA

All the cells of the body are permeable to water, although some of them are permeable only in one direction. If salts were neither added to nor lost from the body, in time, by the absorption and elimination of water, the same osmotic pressure would come to prevail not only in all the cells, but throughout all free liquids of the body. After the exchange between water and the ultimate particles of salts had ended, an equilibrium would everywhere be established between the contents of the cells and the liquid bathing the cell.

This condition of absolute equilibrium of osmotic pressure within the whole organism would cease however, and in fact would cease all at once for the entire system, the instant the osmotic pressure at any one place were changed by the solution or by the deposition of new molecules. If the osmotic pressure in a cell be raised by an increase in the number of molecules dissolved in it, the following phenomena may ensue: (1) if the cell walls are perfectly permeable to salt molecules, the latter in their endeavor to diffuse uniformly will wander out of the cell—i. e., will betake themselves from a place of higher concentration to a place of lower until equilibrium again prevails everywhere; (2) if the cell wall is impermeable to these molecules, then in their endeavor to diffuse they will exert a pressure upon the wall, and water will pass from the surrounding medium into the cell. In this way the liquid in the immediate neighborhood of the cell becomes more concentrated and now acts in turn to draw water toward the periphery of the cell. The movement of water thus set up continues until the difference of pressure becomes too small to be effective. A third case still is conceivable, namely that the cell wall is not absolutely permeable to the salt molecules, but only imperfectly so. Then an emigration of salt molecules and immigration of water molecules will take place simultaneously.

According to the foregoing, the least change in the osmotic pressure of a single cell will result in a movement of substance of some kind. For a complex of cells the currents of the individual cells will be added together if they proceed in the same direction; they will weaken or entirely neutralize each other if they proceed in opposite directions. We must think of the entire organism therefore as permeated by numberless currents and counter currents. Never during life can there be a moment of complete equilibrium, and yet there is a constant endeavor to reach this condition. Thus we might expect *a priori* what is abundantly confirmed by experience, that the osmotic pressures of the different fluids of the body are approximately the same though never exactly so. In the same way the osmotic pressure of the same fluid will not always be uniform, but will vary within narrow limits (Koeppe).

§ 2. INTERNAL SECRETIONS

A. GENERAL

The organs affect one another in many ways by means of their metabolic products. Carried by the blood to all parts of the body, these products act either to heighten or to reduce the activities of the other organs.

The so-called automatic excitation (cf. page 52) by the action of decomposition products of the organs on different parts of the central nervous system is of vast importance in the regulation of the physiological activities of the body, and is to be mentioned first in this connection (cf. also Chapter XXII). For example, when by the activity of the digestive apparatus proteid in increased quantity is thrown into the blood, and the proteid destruction in the body rises as a consequence, the effect in all probability is due to the direct influence of the proteid and its digestive products on the organs—i. e., the activity of the digestive apparatus has brought about an increase in the decompositions of the body without the coöperation of the nervous system (cf. page 99).

Various products of the decomposition of proteid formed in the different parts of the body are carried by the blood to the liver and there are transformed into urea (cf. Chapter XII). With more active destruction of proteid urea is formed in larger amount and this according to our present information stimulates the kidneys to increased activity (cf. Chapter XIII).

The organs act upon one another not only by their katabolic products, but also by substances formed synthetically in some organs, which, entering the blood, profoundly influence the general bodily functions. Such substances, the chemical nature of which is for the most part entirely unknown to us, are formed by the testes, ovaries, thyroid gland, pancreas, and adrenal bodies, probably also by the pituitary body and the kidneys. It is very likely that such *internal secretions* (Brown-Séquard) are formed by other and perhaps by all organs.

Strictly speaking, the enzymes formed in the different organs belong here. Since their importance for the general processes of the body has not been established, we shall not consider them here, but shall merely refer to the facts already cited at page 38.

In the investigation of these internal secretions, workers have often been content to test the action of organ extracts upon the body. This method of experiment of itself, however, does not preclude the possibility that the active constituents of the extract are products of post-mortem changes and have therefore no real significance normally. In order to establish the presence of an internal secretion, one must demonstrate that the venous blood flowing from the organ exercises a specific influence upon the bodily functions, also that the extirpation of the organ produces disturbances which are not due to accidental lesions, and which eventually disappear on transplantation of the organ or upon administration of its extract.

B. THE TESTES

It has long been known that *castration* produces a series of profound changes in both men and animals. A steer which has been castrated loses the vehement strength of the bull and becomes a relatively tractable and quiet animal. If a boy be castrated, his voice does not change as it otherwise would at puberty, but retains more of the high register of the childish voice. The power and endurance of the eunuch's muscles are not those of a fully grown man, but are as a rule soft and flabby. His body frequently has a bloated appearance and becomes very corpulent. The amount of oxygen absorbed also declines after castration. Aside from their sexual functions, which call forth profound physical and psychical phenomena at the time of sexual heat, the testes, therefore, exercise a very marked influence over the entire body.

It might be supposed that this influence is mediated in some way by the afferent nerves of the testes. But even if this were true—and we do not know that it is—still other circumstances would have to be considered. If both testes be removed from a very young cock, and pieces of them be grafted into the abdominal cavity, the secondary sexual characters which are otherwise wanting after castration make their appearance much as usual. Since the testes were in this case entirely separated from their nervous connections, their influence can only be explained from the viewpoint of an internal secretion (Foges).

The compounds given off to the body are probably the same as the active constituents of a glycerin extract of the testis, the subcutaneous injection of which, according to Brown-Séquard, raises the tonus and power of the neuromuscular mechanisms and acts favorably upon the bodily conditions in general.

On the basis of Brown-Séquard's recommendation, testicular extract has found a very extensive use in the treatment of various forms of weakness. It was often assumed that the unquestionably favorable effects were psychical, for it is well known that very often a medicine, of itself absolutely without effect, produces a very marked improvement or even cures all sorts of nervous disorders if only the patient is convinced beforehand that he will be cured. It has been shown, however, by means of experiments, which appear to be entirely trustworthy, that the extract really favors the action of muscular exercise either by raising the power of the neuromuscular apparatus, by diminishing its exhaustibility or by improving its ability to recover. This effect lasts for a long time after the conclusion of exercise and after the injections have ceased, and disappears very gradually (Pregl and Zoth). Even on the isolated heart perfused with blood testicular extract exerts a distinct and powerful effect (Hedbom).

The active substance of the extract has not yet been isolated and is known only in solution. The seat of its action in favoring muscular exercise is not definitely known, but is probably central.

C. THE OVARIES

Just as removal of the testes produces deep-seated changes in the male organism, the failure of the ovarial function, whether by reaching the climacteric or by artificial removal of the ovaries, is signalized by a series of disturbances—cardiac palpitations, sweatings, vertigo, and the like—which cannot be due to the cessation of the sexual activity alone. Since an ovary completely isolated from its nervous connections, and engrafted into some other part of the body, prevents the atrophy of the other sexual organs, including the mammary glands, and prevents the failure of menstruation (Halban), it is evident that the influence here spoken of cannot be due exclusively to the nervous relationships of the organ, but that we have to do again with an internal secretion, the removal of which causes the disturbances alluded to.

It is often stated by gynecologists that castration of the woman, exactly as in man, is in many cases followed by pronounced corpulency, which indicates that metabolism declines after the operation. This conclusion is confirmed by a series of experiments on fasting dogs by Loewy and Richter. After removal of the ovary the consumption of oxygen fell on the average twelve per cent, whereas feeding the castrated females with ovarial substance raised the metabolism again, in some cases above the original level. The ovarial substance has no influence on the metabolism of normal, noncastrated male or female animals; but on castrated male animals its action is intense.

How this substance raises metabolism, whether because of an increased muscular tonus, or muscular activity, or in some other way, nothing can be said at present. We only know that the destruction of proteid appears to suffer no change under its influence.

D. THE THYROID GLAND

Exact knowledge of the physiological purpose of the thyroid gland dates properly from 1882, when J. L. Reverdin drew attention to the profound disturbances which follow total extirpation of the gland for goiter. Shortly afterwards Kocher and Reverdin pointed out the great similarity of these changes with the complex of symptoms which was first described by Gull (1873) and named by Ord *myxœdema.*

The contribution of Reverdin induced Schiff to take up again certain experiments on the extirpation of the thyroid in dogs which he had carried out as far back as 1856, but which had remained unnoticed. Out of 60 dogs operated on by Schiff, 59 died within four weeks. From this time on spirited efforts were made to throw light on the function of the thyroid gland, and all observers reached the same result: that its removal from the dog led to a fatal end within a few days or weeks; that in man its removal caused very considerable disturbances in the nutrition of the body; also that younger individuals succumbed to the operation more quickly than older ones.

It has sometimes been assumed that the resulting symptoms, which will be discussed more fully presently, are caused by the incidental effects of the operation. But this is certainly not correct. The whole operation can be carried on in the roughest possible manner, and the animal will show none of the characteristic symptoms if one fails to remove the glands (Fano). If only a part of the gland is left the symptoms do not appear, but hypertrophy of the part remaining takes place. The disease of myxœdema in man also speaks against such a view. And, finally, it is controverted absolutely by the fact that *intraperitoneal grafting* protects the patient from the consequences of thyroidectomy so long as the transplanted gland continues to be functional (v. Eiselberg); if it atrophies, the usual symptoms appear.

Likewise by *subcutaneous injection* of thyroid extract, as well as by *administration* of thyroid preparations by the stomach (Howitz), the same favorable effect is obtained—i. e., the harmful effects of the removal of the thyroid can be prevented by artificially introducing thyroid substance into the body.

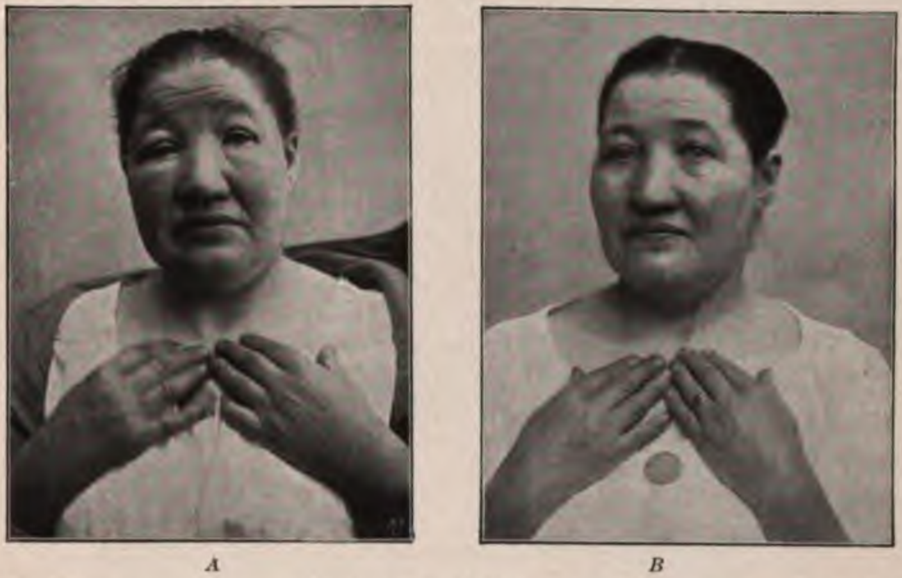
A *B*

FIG. 137.—A myxœdematous woman, after J. A. Andersson. *A*, before treatment. *B*, after seven months' treatment with thyroid extract.

It happens exceptionally that a dog, after extirpation of the thyroid, is not attacked by the usual symptoms. In this case there are probably accessory thyroids which have taken up the function of the main gland.

The disturbances appearing after extirpation of the thyroid affect the most widely different organ systems of the body. We shall now summarize them briefly with special reference to their appearance in man.

The skin, especially of the head and face, becomes greatly swollen (Fig. 137, A) because of an accumulation of mucin in the subcutaneous connective tissue. In later stages of the disease the mucin decreases, and atrophic changes of the connective-tissue fibers appear along with general emaciation. The skin becomes hard, rough and dry; its secretion ceases; the hairs change and fall out; the visible mucous membranes become swollen; and the voice becomes harsh and monotonous. The internal organs exhibit marked pathological changes;

the kidneys and the liver undergo fatty and colloidal degeneration, and the arterial walls a hyaline degeneration.

Metabolism is abnormally low; in one of the patients investigated by J. A. Andersson it amounted on the average to only about 1,200 Cal. per day—i. e., 18.8 Cal. per kilogram of body weight. The appetite is poor and the utilization of foodstuffs is below the normal. On the other hand no noteworthy change is observed in the rate of the pulse.

The disturbances of the nervous and muscular systems are very marked. In the monkey the individual contractions of the muscles succeed each other after the usual manner of clonic convulsions; then comes a summation of contractions and after this tetanuslike spasms, ending finally in complete rigidity and contracture. Besides these, indications of reduced nervous activity occur in the form of paralysis and anæsthesia. Thyroidectomy not infrequently brings on functional neuroses, such as epilepsy, etc. These disorders are not of peripheral origin, for they are wanting after section of the motor nerves; on the other hand they are not abolished by scraping off the motor zone of the cerebral cortex. The point of discharge of impulses for the muscular convulsions appears therefore to lie in the lower parts of the central nervous system, although the higher nerve centers are not in a perfectly normal condition, as judged by histological appearances after extirpation of the thyroid. This appears

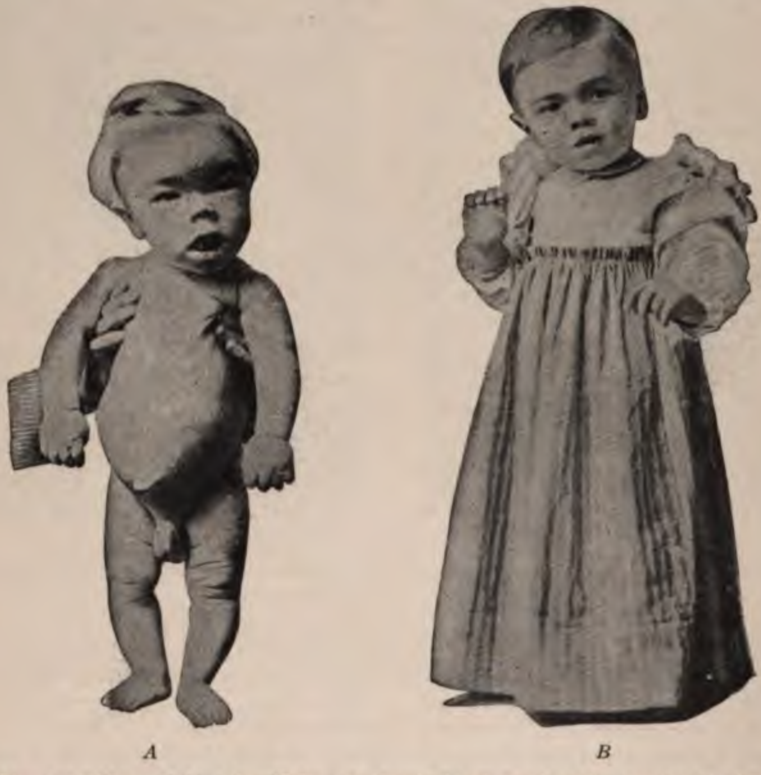

FIG. 138.—A cretinous child, after Holt. *A*, twenty-three months old, previous to treatment. *B*, after six months' treatment with thyroid extract.

also from the fact that the motor cortical fields soon become fatigued by electrical stimulation, until in the later stages of the disease, when the voluntary movements become extremely slow and imperfect, stimulation produces no visible effect at all. The same is true also with stimulation of the corona radiata and of the spinal cord. At the height of the convulsions, on the contrary, the excitability of the entire nervous system is plainly increased.

Again, all those parts of the brain which are active in the psychical functions become functionally reduced by extirpation of the thyroid. In myxœdematous patients we meet with weak memory, extreme irritability, stupidity, etc., which in turn find expression in a decline of muscular tone and in the vigor of the bodily movements generally.

Finally, disturbances in the temperature and the heat regulation of the body are seen. A considerable rise in temperature has very often been observed during the height of the muscular convulsion; but when this stage has passed a decided fall ensues—in the monkey to 33°. In man also the subnormal temperature is one of the most constant symptoms, and the patient feels cold.

In the growing organism after suppression of the thyroid, the bones fall considerably behind in their development and the ossification of the epiphysial cartilages and synchondroses is delayed materially. The psychical disturbances are probably more pronounced also than in grown persons (Fig. 138).

Most of these disorders gradually disappear after treatment with preparations of thyroid. The skin acquires again a normal appearance (Fig. 137, B); metabolism increases—in the above-mentioned case, reported by Andersson, after nine months' treatment it had returned to the normal value of 2,099 Cal. = 32.3 Cal. per kilogram of body weight; the utilization of foodstuffs is more complete; the muscular and nervous disorders are reduced, and in young individuals one can often observe with this treatment absolutely brilliant results (Fig. 138, B).

From all this it follows that the thyroid gland must be regarded as an organ which, by internal secretion of certain substances, performs a *vitally important function.* These substances represent either important constituents of the liquids of the body, or are used for the neutralization of poisons which may be present. We cannot say definitely whether the thyroid has still other functions or not.

From histological investigations of the process of secretion in the thyroid, we appear to be justified in the assumption that the follicular contents are elaborated by the epithelium surrounding the follicle; and that it passes through openings in the wall of the follicle—formed by simple atrophy (colloidal fusion) of the epithelial cells—from the cavity of the follicle into the lymph spaces of the gland. In the lymph spaces the contents are gradually diluted with lymph; the secretion soon loses its characteristic consistency and ability to take stains, and is added to the general circulation through the lymph vessels (Hürthle).

Our knowledge of the *innervation* of the thyroid is still very imperfect. According to Exner, Jr., after section of the thyroid nerves of the cat on one side, when the opposite half of the gland has been removed, various disturbances (hyperæsthesia, apathy, convulsive twitchings, etc.) appear during the first few days, but disappear completely within a few weeks. How far these disturbances are the direct result of the loss of nervous control, or whether they are due to other circumstances, can scarcely be decided at present. Hürthle and Katzenstein were unable to produce any histological changes by *stimulation* of the thyroid nerves. The latter succeeded, however, in demonstrating distinct signs of degeneration in the thyroid of the dog after section of its nerves.

Recently attempts have been made in many ways to isolate the active substance of the thyroid, and the *iodothyrin* produced by Baumann has been the special object of numerous investigations.

Iodothyrin is a brown-colored, amorphous substance which on heating swells up enormously and is decomposed, yielding an odor suggestive of the pyridin bases. It is almost insoluble in water, and is soluble with difficulty in alcohol. It dissolves readily in dilute alkalies and is precipitated again on addition of acids. Concentrated caustic soda with heat decomposes it slowly. The gland can be boiled for days in a ten-per-cent sulphuric acid without destroying its iodothyrin.

This substance gives none of the proteid reactions, but always contains phosphorus in organic combination (0.56 per cent P) and, what is most important, at least 9.3 per cent iodine. Notwithstanding that it occurs in the thyroid gland to the extent of only 0.3 per cent, iodothyrin has a marked effect on the symptoms following the suppression of the thyroid, even when administered in very minute quantities.

According to Baumann, iodothyrin occurs in the gland in combination with proteid; and Ostwald has reached the conclusion that the so-called colloid of the thyroid gland consists of two proteid bodies, only one of which, the thyreoglobulin, contains iodine; the other is a nucleoproteid containing a carbohydrate group. By boiling the former with ten per cent H_2SO_4, Ostwald isolated a product containing 14.3 per cent I, which he regards as an extremely pure iodothyrin.

The entire yield of this substance calculated on the basis of iodine is, however, only about one-tenth of the iodine in the gland, and it is therefore doubtful, as Blum and Tambach have remarked, whether iodothyrin occurs as a conjugant with proteid in the gland, or whether it is not first split off by destruction of the proteid molecule.

A fuller presentation of the views expressed by different authors concerning the nature and the mode of action of the thyroid substance is impossible here. We may mention only the fact that S. Frankel, as well as Drechsel and Kocher, Jr., have isolated two other substances of a basic nature which exert a well-marked, though not very strong, favorable action on animals whose thyroid has been removed.

If a healthy animal be fed with a great quantity of thyroid, various symptoms of poisoning make their appearance, such as tachycardia, polydipsia, polyphagia, polyuria; the quantity of urea increases, sugar appears after some time in the urine, and the animal falls off in weight. Likewise in men when thyroid is administered as a medicine, in too large doses, excitement, abnormal sensation of heat, increased destruction of proteid, jaundice, albuminuria, cardiac palpitation and cardiac weakness make their appearance.

E. THE PANCREAS

When the pancreas of a mammal (dog, cat, pig) is totally removed without any accidental lesions, *a severe diabetes* (according to some authors invariably, according to others generally) ensues (v. Mering, Minkowski, de Dominicis, 1889).

The appearance of *sugar in the urine* does not always show immediately after the operation. It appears sometimes sooner, sometimes later, but invariably increases in intensity within the next twenty-four hours, and as a rule also on succeeding days. In most cases on the first day there are found only traces, up to one per cent; on the following day from four to six per cent; and only on the third day does the sugar elimination reach its maximum of eight to ten per cent and over. If now food be not given, the quantity of sugar in the urine begins gradually to fall off; but it does not disappear altogether after seven days of fasting. With a plentiful supply of food the sugar in the urine may amount to ten or twelve per cent, and the daily quantity of sugar eliminated by a dog of 15 kilos on a pure meat diet may reach 102 g., and on addition of carbohydrates may reach a still higher value.

From these observations it is clear that the pancreas is extremely important for the normal *decomposition of the carbohydrates* of the body. But it is conceivable that the effects described are due to some accidental lesion attending the operation. This is opposed by the following experimental facts. If a relatively small piece of the gland be left in the abdominal cavity, diabetes does not occur, notwithstanding that the operative procedure is the same. Further, if in the operation a piece of the gland be grafted under the abdominal skin in such a way that it remains in vascular connection with the abdominal cavity, and after it has become healed in, the rest of the gland left in the normal position be removed, the animal does not become diabetic, nor does diabetes result from section of the vascular stalk to the subcutaneous graft. But sugar appears in the urine immediately and in large quantities, and the sugar content in the blood rises considerably, as soon as the subcutaneous graft is removed, although the operation for its removal is quite an insignificant one. We must conclude that neither the operative lesions nor the absence of the pancreatic secretion from the intestine can be the cause of the sugar elimination. The pancreas therefore exercises a *specific influence* on the transformation of sugar in the body.

The pancreas may be made to waste away by gradual injection of fat or of acids into the duct of Wirsung. When this is done in the dog, in many cases no sugar appears in the urine (Hédon, Rosenberg). To explain these remarkable facts, we are almost compelled to assume that some other organ has taken over the function of the pancreas in the metabolism of sugar, and that this can only happen in case the function of the pancreas is abolished very gradually. The most natural explanation, namely that portions of the pancreas remain intact, is excluded by the express statements to the contrary of the authors themselves who report these experiments.

How are the phenomena which follow extirpation of the pancreas *to be explained?* Even under normal circumstances with a very large amount of sugar in the food, a part of it passes out in the urine (alimentary glycosuria). Different kinds of sugar behave differently in this respect. Levulose is almost all burned, while cane sugar, grape sugar and especially milk sugar pass over in relatively large quantities into the urine. After extirpation of the pancreas, much larger quantities of sugar than usual are found circulating in the blood; it is evident, therefore, that sugar must also appear in the urine.

The different carbohydrates fed to an animal whose pancreas has been removed behave very differently. On feeding grape sugar the entire quantity fed appears in the urine. Maltose is transformed into dextrose and as such is eliminated. On the other hand the lævorotatory carbohydrates (levulose, inosit) are used by the body, although they are in part transformed into grape sugar and are excreted as such. After feeding with cane sugar, neither cane sugar itself nor levulose are to be found in the urine; instead there always appears a considerable increase of the dextrose output. Presumably therefore the cane sugar is inverted, and besides the usual dextrose arising from it, a part of the levulose also leaves the body as dextrose. Milk sugar also appears to be transformed into grape sugar and to be eliminated as such.

The *glycogen* disappears from the liver of animals made diabetic in this way, down to the last traces. But in animals in which parts of the pancreas have been left in the abdominal cavity, fairly large quantities of glycogen are still found. Finally, after feeding levulose, there occurs under certain circumstances a considerable deposit of glycogen in the liver, and, what is especially noteworthy, this glycogen is dextrorotatory as usual.

After suppression of the pancreas, therefore, *the power of the body to form glycogen* or fat from dextrose is destroyed. Such animals show an increased destruction of tissue proteid, which is most clearly attested by the fact that in spite of an excessive supply of food, they very rapidly become emaciated, losing in two weeks as much as one-third or more of the body weight. That is, they live principally at the expense of their own bodies. Since, in spite of this, sugar is eliminated in large quantities in the urine, the organism must have lost the ability to burn sugar to the usual extent.

The consequences of removing the pancreas make it evident, therefore, that this organ plays *an essential part for the storage of carbohydrates* in the body, for their transformation into fats, and for the combustion of sugar.

In explanation of these effects of the pancreas on the transformation of sugar, one might conceive either that a substance is formed in the gland which is necessary for the normal metabolism of sugar, or that the gland destroys some substance formed elsewhere, the retention of which in the organism would produce the effects described. The former of these suppositions appears the more probable, although there is scarcely yet to be found any binding proof of it, and nobody has so far succeeded in obtaining the active substance from the pancreas. It appears from some facts not presented here that the discharge of this substance into the blood is under partial control of the central nervous system.

F. THE ADRENAL BODIES

In 1855 Brown-Séquard announced that *bilateral extirpation of the adrenal bodies* resulted fatally within a short time after the operation. Later experiments have on the whole confirmed this statement. Death follows within a few hours or days at most. If the organs are removed in several operations, portion at a time, the animals (cats) die somewhat later. If some time be allowed to elapse between the operations for the two sides, the animal (rabbit) may exhibit no abnormal symptoms within a month.

After *extirpation of one adrenal body* and a part of the other, animals may continue to live, though in a reduced state of health, for some time after the operation. They are more sluggish than usual, they quickly become fatigued by muscular efforts, and the body rapidly falls away in weight.

These conditions gradually pass away and the animals recover. When only a part of one adrenal body is left in position, regeneration of its substance takes place, just as, after unilateral extirpation, a compensatory hypertrophy of the one remaining appears. In both man and animals accessory adrenals are found which are sufficient to maintain life after total extirpation of the main bodies.

Hultgren and O. Andersson describe the *abnormal phenomena appearing after the removal* of the adrenals as follows: The animal recovers from the operation within a few hours, and aside from a poor appetite or none at all, shows no unfavorable symptoms within the next few days. During the last twenty-four hours before death, or still earlier when the symptoms run a slower course, the animal becomes dull and stupid, most of the time sits perfectly quiet and, what is particularly striking, in cats, exhibits weakness and uncertainty in the movements of its hinder extremities. At the same time the temperature begins to fall, and as this continues the general listlessness and weakness of the animal increases. Cats lie most of the time with the nose on the floor, and with eyes half-closed follow what is going on about them, but not with the usual interest. They react to stimuli more feebly and more slowly than before. They walk unsteadily and with a peculiar stiffness of the hinder legs. In leaping down from a chair they are likely to fall in a heap. They become fatigued with very slight movements, and lie for a long time deeply exhausted. This loss of strength continues more and more and finally dyspnœa sets in; respiration becomes deep and slower; the heart becomes less frequent and irregular, and death ensues. Convulsions rarely occur in cats and dogs, but in rabbits they are fairly common.

Among other conditions observed on such animals the following may be mentioned. Neither digestion, nor the combustion of proteid, nor the content of hæmoglobin in the blood, nor the number of red blood cells is influenced by the operation. No paralyses are to be observed and the electrical excitability of the nerves remains unchanged to the time of death.

The blood pressure falls immediately after the operation and in the last few hours reaches a very low level.

The blood of the operated animals is said to have a pronounced toxic action. Thus if blood from one operated animal be injected into another whose adrenals have also been removed, the symptoms which would otherwise not appear for several hours come on within a short time.

The profound effects of the removal of the adrenals cannot be caused by the operation alone nor by accidental lesions. This we know from the observation that portions of the adrenals which have been left unintentionally suffice to keep the animal alive; also from the fact that no disturbance occurs if the adrenals be separated from all their connections except those with the vascular system.

The evil effects of the extirpation of the adrenals are therefore *due to the loss of some function* which is important for the whole body. This function may be one of two kinds: either they destroy some product or products formed in metabolism which, when present in larger quantity than the normal, poison the organism, or they form substances which are necessary for the normal activities of the body. The results of extirpation, and especially the influence set up by the injection of the blood of one animal deprived of its adrenals into another animal operated on in the same way, appear to speak rather definitely for the former supposition. Even if this were correct, however, the physiological purpose of the adrenals would not be wholly explained thereby, for injection of adrenal extract or of blood from the adrenal vein (Cybulski) into animals which have lost their adrenal bodies produces a marked improvement in the symptoms for some time, and has an unmistakable effect on perfectly normal animals. The conclusion which seems to be inevitable is that *the adrenals give off to the blood* one or more *specifically active substances.*

These substances are dialyzable; soluble in water, dilute alcohol and in glycerin, but insoluble in absolute alcohol and ether; withstand drying at 110° C. and boiling, if not too prolonged. They are destroyed by alkalies, but not by acids. Numerous attempts have been made to isolate and identify this substance. According to v. Fürth, it is related to the pyridin series and contains a ring nucleus with two hydroxyl groups in the ortho position (adrenalin). It has an alkaline reaction and forms salts with the acids. Its empirical formula, according to Takamine, is $C_{10}H_{15}NO_3$, according to Abel $C_{10}H_{13}NO_3. + \frac{1}{2} H_2O$. The percentage of this substance in the adrenals is said to be about 0.1–0.17 per cent.

If the extract be injected directly into a vein, it acts powerfully in very small quantities. Thus Takamine obtained a distinct rise of pressure by injecting 0.0000013 g. of adrenalin. The chief effect of such an injection of this extract is a *sudden rise of blood pressure.* This is due in part to an augmented heart action which can be demonstrated also on an excised heart or heart muscle, and in part to a powerful contraction of the smaller arteries caused by a direct action of the extract on the musculature of the vessels. According to Cyon, the vasomotor center in the medulla and the cardiac inhibitory center are excited. The slowing of the heart beats observed by many authors, which do not appear after section of the vagi (according to most authors), is said to be a direct effect of the injection and the result of a sudden increase of intracranial pressure.

Most of the effects of injection of adrenalin *last only a few minutes,* and then gradually disappear. This temporary character might be due either to a transformation of the adrenalin taking place in the blood stream, or to its removal from the vessels. Adrenalin is eliminated in the urine only in very small quantities.

When injection is made subcutaneously in animals from which the adrenals have been removed, it produces a rise during the premortal fall of temperature, and improves the general bodily condition of the animals. They become more active, the weakness and uncertainty of their movements are diminished and they leap with much more vigor than before. After repeated injections, however, the effect fails, and it is possible to prolong the life of the animal in this way for only about twenty-four hours (Hultgren and O. Andersson). On administration of very large quantities of adrenalin to normal animals, especially after intravenous injection, profound toxic effects ensue which result fatally.

With regard to the *influence of the nervous system* on the formation and secretion of the active substance of the adrenals, Biedel and Dreyer state that stimulation of the splanchnic below the diaphragm produces, quite independently of the alterations in the blood flow, a copious secretion of it into the blood.

G. THE PITUITARY BODY

On the basis of anatomical and embryological facts most authors assume a close physiological relationship between the *hypophysis cerebri*—i. e., anterior part of the pituitary body—and the thyroid gland. This supposition is supported by the facts, to this extent at least, that hypertrophy of this structure has been observed in animals after extirpation of the thyroid, and in men suffering from myxœdema. A satisfactory explanation of this relationship has not yet been found.

Recently many experiments have been made on the effect of injecting *extract of the hypophysis* into the circulation, and a distinct action upon the heart and blood vessels has been obtained. According to Schäfer and Vincent, we have to do here with two different substances, which are distinguished chemically by their solubility in alcohol and ether, one being soluble, the other not.

The former brings about a very temporary fall in the arterial blood pressure. The other increases the blood pressure, slows and strengthens the heart beat and produces a marked diuresis. The effect is tolerably permanent, although it becomes less and less with successive injections. From experiments on the isolated heart or heart muscle it appears that this influence extends to the peripheral end apparatus of the cardiac nerves. Other observations indicate that the extracardial center also is stimulated (Cyon). The vasomotor nerves behave in the same way: on the one hand the vessels contract after destruction of the medulla (Oliver and Schäfer); on the other, the vasoconstriction occurs if the extract is injected into the brain vessels only (Cyon). In Cyon's opinion the effects of an extract on the heart and on the vessels depends upon two different substances.

Curiously enough the substances which produce this effect upon the circulation, according to Howell, Schäfer, and Vincent, are, for the most part at least, not contained in the anterior glandular part of the pituitary body, but in the posterior infundibular part. However, this section of the pituitary body also contains glandular epithelial cells, which surround cavities filled with a colloidal substance (Berkley).

From results thus far before us no positive conclusion can be drawn as to the normal working of the hypophysis.[1] It is conceivable that the substances obtained by different methods from the gland are normally formed there and are given off to the blood. But it is also possible that they represent products of decomposition which are formed post mortem only, in the methods of extraction.

A definite choice between these two possibilities is not yet possible, since from the many conflicting statements as to the results of extirpation, we cannot tell certainly whether any disturbances follow loss of the hypophysis alone.

H. THE KIDNEYS

Certain observed facts indicate that the kidneys not only remove different products of decomposition from the body, but give off to the blood one or more substances which are of service in the body. When the kidneys are removed from an animal, or are rendered functionless in man, within a few days symptoms of severe uræmic poisoning make their appearance. The most natural assumption is that the symptoms are caused by the retention of the products otherwise eliminated. But it has been observed that patients who suffer with anuria for weeks may not show any signs of uræmia. Brown-Séquard explains this failure of abnormal results by supposing that only the excretion of urine, but not the production of the "internal secretion" of the kidneys, has ceased. In support of this view he carried out experiments, in which animals whose kidneys were removed and which showed the uræmic symptoms were very much benefited by injection of an aqueous extract of kidney. Moreover E. Meyer has shown that nephrectomized animals which exhibited the periodic respiration resulting from uræmia, again began to breathe normally after intraperitoneal injection of a kidney extract or intravenous injection of blood of a normal animal. Other authors have reached entirely negative results with similar experiments. The view of Brown-Séquard therefore cannot be regarded as by any means established in fact.

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[1] Fischera has reported quite recently that castration of cocks, guinea pigs and rabbits produces a marked hyperplasia of the hypophysis. The change in the capon is very sudden and can readily be recognized in microscopical sections of the part. Injection of testicular extract just as quickly abolishes the hyperplasia or prevents it altogether.—Ed.

I. THE SPLEEN

Extirpation of the spleen produces no serious effects; it is therefore not a vitally important organ. According to Schiff and Herzen, the spleen is in some way concerned in the formation of trypsin from the zymogen formed in the pancreas, and this has recently been confirmed by Gachet and Pachon (cf. page 252). The quantity of bile pigments formed in the liver is also said to fall considerably after extirpation of the spleen (Pugliese). This is in line with the view arrived at by many authors, and latterly by Jawein, that the spleen removes from the blood and transforms the worn-out red blood corpuscles.

An intravenous injection of splenic extract at first lowers the blood pressure and later raises it slightly; it also appears to be able to regulate the rhythm of the excised heart. Again, it is said to have the same effect as an infusion of red bone marrow in raising the number of red blood corpuscles and the content of hæmoglobin in the blood (Danilewsky).

Since we have no data as to the effect of the venous blood from the spleen, these results furnish no definite point of vantage for the explanation of the physiological purpose of this still very enigmatical organ.

CHAPTER XII

THE FINAL DECOMPOSITION OF FOODSTUFFS IN THE BODY

As already mentioned at page 27, the foodstuffs in their combustion do not pass over immediately into their end products, but are gradually split up into simpler and simpler substances, oxidation and reduction processes probably succeeding each other in rapid succession. In order to secure more light on these processes, investigators have studied the transformations which organic substances, more or less closely related to the foodstuffs, undergo in the body. Important as these investigations are, and significant as are the results which we expect from this field in the future, we must limit ourselves here, for want of space, to the transformations of the true foodstuffs. Unfortunately our knowledge of these subjects is still very imperfect and the views of authors are considerably at variance with one another on many of the most important points.

§ 1. THE FINAL DESTRUCTION OF PROTEID

In its digestion in the alimentary canal, proteid is for the most part split up into relatively simple products. To what extent it is absorbed in the form of albumoses and peptones we cannot say definitely. Nor is anything known concerning the extent to which synthesis of proteid from the end products just named eventually takes place in the body. If the proteid is not stored, both the primary and the final digestive products are still further decomposed until the elements of proteid are ready to be eliminated as carbon dioxide, water and urea.

Formerly it was supposed that proteid in its decomposition is split up into a nitrogenous and a nonnitrogenous portion. This view however is no longer tenable, for from the fact that numerous nitrogenous compounds appear successively in the hydrolytic cleavage of proteid, it follows that the final separation of the carbon from the nitrogen takes place at a very late stage of the process.

In the body proteid and its digestive products do not undergo a continuous, progressive cleavage by oxidation. There undoubtedly occur a number of synthetic processes by which the groups contained in the proteid molecule undergo many changes of position of one kind and another. Hence, the problem of the decomposition of proteid in the body is extremely complicated and cannot be regarded as by any means solved.

In the destruction of proteid by chemical reagents outside the body a certain quantity of urea is formed, which comes from arginin, not by oxidation, but by cleavage of the arginin with absorption of water into urea and diamino-valerianic acid (Drechsel).

Drechsel estimated that 100 parts of proteid undergoing cleavage in the body would be able to yield in this way 3.8 parts of urea without suffering any oxidation. Since, further, 100 parts of proteid yield altogether 34.3 parts urea, it follows that about one-ninth of the total urea eliminated may issue from the proteid by a simple process of cleavage. In fact we always find in all animals, even in those in which the greatest part of the nitrogen of the urine appears as uric acid, a certain quantity of urea (cf. pages 70 and 75 for the arginin content of the different proteids).

But by far the greatest part of the urea eliminated arises from proteid by processes of oxidation. When amino acids (glycocoll, leucin, aspartic acid) are digested with finely ground, fresh organs, ammonia is split off from them (Lang). In the mammals these compounds as well as ammonia are transformed into urea and as such are given off through the kidneys (Nencki, Salkowski *et al.*). It is conceivable, therefore, that ammonia represents an intermediate stage in the formation of urea. Since, however, both ammonia and the above-mentioned amino acids contain only one atom of N in the molecule, and urea contains two, the latter can only be formed from the former by a process of synthesis. This might take place by the combination of ammonia with carbon dioxide into carbamic acid or ammonium carbamate, and the formation of urea from these by the loss of water. In fact,-Drechsel succeeded in preparing urea by subjecting an aqueous solution of ammonium carbamate to electrolysis with an automatic commutator in the circuit, so that the salt was alternately exposed in rapid succession to oxidation by nascent oxygen and reduction by nascent hydrogen. The processes taking place are illustrated by the following scheme:

$$\text{I. } \underset{\text{ammonium carbamate}}{NH_2.CO.O.NH_4} + O = NH_2.CO.O.NH_2 + H_2O$$

$$\text{II. } NH_2.CO.O.NH_2 + H_2 = \underset{\text{urea.}}{NH_2.CO.NH_2} + H_2O$$

The fact that carbamic acid can be demonstrated in the blood and in the urine constitutes a strong argument for this view.

The formation of urea might also take place by the union of an amido residue, $CONH_2$, at the instant of its formation, with the amidogen, NH_2, arising by oxidation of ammonia (Hofmeister).

A definite decision between these two possible explanations is not to be had at present; besides, it is not at all certain that the formation of urea takes place by one method only.

Concerning the *seat of urea formation*, we can think of two possibilities: either it is formed in all parts of the body wherever proteid is broken down, or certain organs have the function of transforming the intermediary products of metabolism into urea. After removal of the kidneys urea collects in the body [illegible] s; these organs cannot therefore play an all-i[illegible]. Meissner found in the liver of the dog l[illegible] blood, and so designated this organ as [illegible] urea of mammals originates.

This view received substantial support in the experiments of v. Schroeder, in which by artificial perfusion of an excised dog's liver with ammonium carbonate or formate, the production of urea from these salts was demonstrated directly. Experiments carried out in the same way on the kidneys and muscles gave only negative results. Likewise by digestion of glycocoll with crushed liver tissue or liver extract, urea, or, to be more exact, a closely related compound is formed (Richet, Loewi *et al.*).

Indirectly the importance of the liver in this connection is shown by the experiments of Nencki and Pawlow on dogs with an Eck fistula between the portal vein and the inferior vena cava (cf. page 274) in which the liver therefore received its blood by the hepatic artery only. In these animals the elimination of ammonia in the urine increased and the power of the organism to form urea from carbamic acid introduced into the stomach was lost. After a time characteristic abnormal symptoms made their appearance (namely, somnolence, ataxia, excitation, loss of vision, epilepsy, anæsthesia, tetanus) and these could be produced at will by an abundant supply of nitrogenous food, ammonium salts, or glycocoll.

In *birds and reptiles* the nitrogen of the decomposed proteid leaves the body chiefly as uric acid. Any information we can get as to the seat of uric acid production in birds ought therefore to be strongly suggestive of the seat of urea production in mammals. Birds are especially well adapted to experimental investigation of this subject because extirpation of the liver is relatively easy on account of the peculiar relations of the circulation. The animals live for as much as twenty hours after the operation. Their urine, however, is very poor in uric acid, since only about three to four per cent of the total nitrogen is now eliminated in this form, whereas the percentage of ammonium salts (lactate) is considerably increased. Amino acids, which normally are transformed into uric acid in birds, when fed to geese deprived of the liver, are eliminated as ammonium lactate. Urea passes out unchanged (Minkowski). The quantity of uric acid eliminated also has been increased by electrical stimulation of the liver (Milroy). Hence the liver must be regarded as the seat of uric acid production in birds.

We may conclude also that *urea is formed* from ammonia to a very large extent *in the liver*, and that the other organs probably have at most only a small share in this function. The digestive tract is indicated as the chief source of the ammonia; for, according to the investigations of Nencki, Salaskin and others, the percentage of ammonia in the intestinal and gastric mucosa is considerably greater than that of the other organs; the portal blood also is considerably richer in ammonia than the blood of the hepatic arteries and veins. The ammonia split off in the liver from the amino acids must be taken into account also.

There is in all this however no proof that all of the urea, exclusive of that split off directly from the proteid (cf. page 369), comes from ammonia and is formed in the liver. Observation shows rather that in the dog large quantities of urea are eliminated even *after complete extirpation* of the liver. Similarly it has been found that in diseases of the human liver where the entire organ, to judge from examination of sections, had become completely inefficient, more than sixty per cent of the total nitrogen in the urine has been excreted as urea. Now if it be true that only the liver can transform ammonia into urea, it follows that only a part of the nitrogen contained in proteid passes over into ammonia, while another part runs through other stages until finally it also is given off from the body as urea.

Under normal circumstances ammonia in certain quantities is always present in the urine. This ammonia is necessary in order to help saturate the acids excreted in the urine, for the fixed bases are not sufficient for this purpose. If the acid production in the body is large, or if free acids are taken into the body, the quantity of ammonia is larger and the quantity of urea correspondingly decreases. With increased supply of fixed alkalies the quantity of ammonia falls, and the quantity of urea rises. The formation of urea from ammonia varies therefore according as a greater or less amount of ammonia finds employment as such. It appears to follow from what has already been said that the regulation of this function is committed to the liver.

The *uric acid* which is eliminated from mammals in general does not represent a product of proteid decomposition, but appears to come mainly from the nucleins (Horbaczewski). The nucleins are split up in the body into proteid, phosphoric acid and purin bases (cf. page 76). The latter pass by oxidation over into uric acid; however, some purin bases besides uric acid occur in the urine, though the quantity of these is rather small.

Recent observations (Burian and Schur, Sivén) have proved that uric acid is derived in part from purin bases which are introduced into the body with the food (exogenous), and in part from those present in the body itself (endogenous).

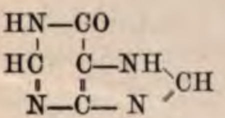
The amount of the latter is constant for the same individual—for an adult man in health amounting to 0.3–0.6 g. (=0.1–0.2 g. N) per day. It can be determined directly if a diet containing no nucleins (purin bases)—consisting for example of milk, cheese, eggs, potatoes, rice, white bread, etc.—be given. The amount of purin bases and of uric acid in the urine is then relatively constant, notwithstanding that very great variations in the quantity of proteid may be supplied in such foods. We have no positive information yet as to the processes upon which the so-called endogenous acid depends.

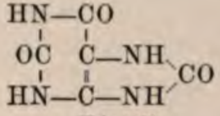
If, however, the diet consist of foods which contain purin bases (meat, liver, thymus, etc.) the quantity of uric acid eliminated increases in proportion to the amount of purin eaten. The amount of any purin base that will appear in the urine as such, or as the closely related uric acid, depends upon its chemical nature. Thus with hypoxanthin (meat, liver, spleen) one-half, and with adenin (thymus) one-fourth of the purin nitrogen fed appears again in essentially the same form in the urine (Burian and Schur).

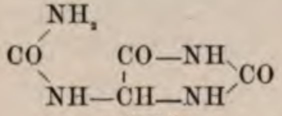
According to the investigations of Wieners, uric acid is formed at least in the liver, the thymus and spleen, and it is not unlikely that all the organs participate in its production according to the quantity of nucleins contained in them.

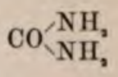
At any rate, the purin derivatives given off in the urine of mammals is only a fractional part of that taken up in the food, or of that formed in the body itself. A considerable part of both must be further oxidized and be transformed into urea. Probably the best proof of this is the fact that after extirpation of the kidneys, uric acid does not accumulate in the blood. Hence the normal elimination of uric acid might be due to the circumstance that the transformation of urea is not quite complete, but the blood takes the opportunity presented during its passage through the kidneys of partially ridding itself of waste in the form of uric acid.

Allantoin appears in the urine of the dog after ingestion of uric acid (Salkowski). It has been demonstrated also in the urine of man—e. g., in hepatic cirrhosis. This compound might, therefore, represent an intermediary step in the destruction of uric acid. The genetic relationship between the substances considered here will be evident from the following formulæ:


Hypoxanthin
(6-Oxypurin)


Uric acid
(2, 6, 8-Trioxypurin)


Allantoin
(Glyoxyl-diureïd)


$CO\left\langle\begin{array}{l}NH_2\\NH_2\end{array}\right.$

Urea
(Carbamide)

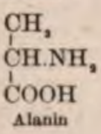
It appears from several observations that the *liver is the seat of the destruction of uric acid.* By artificial perfusion of this organ with blood, or by digestion of uric acid with ground liver substance, uric acid disappears. Moreover, according to Burian and Schur, it immediately appears in the blood of nephrectomized dogs when the liver also is thrown out of the circulation. And yet there are other observations which go to show that other organs also are capable of decomposing uric acid.

Uric acid therefore represents an *intermediary product* of metabolism in Mammalia. In birds it is the chief nitrogenous end product of proteid, and is formed for the most part by a synthetic process carried to completion in the liver. A residue of urea and sarcolactic acid are probably to be regarded as the basal material of this synthesis.

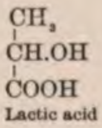
The *sulphur* contained in proteid is eliminated in the urine mainly as sulphates and ethereal sulphates ("acid sulphur"), but in part also as "neutral sulphur" (sulpho-cyanic acid, derivatives of taurin, cystein, oxyproteïc acid, and other organic compounds). A part of the sulphur moreover is given off as taurocholic acid in the bile (cf. page 253). It is likely that this sulphur comes mainly from the cystein group.

As mentioned at page 127, it is very probable that under certain circumstances at least, carbohydrates are formed in the body from proteid, and, indeed, that this may take place without the participation of the carbohydrate group contained in most proteids. From all that we know of the manner of cleavage of proteids, this formation of carbohydrates must be regarded as a synthetic process, in which sugar is constructed by splitting off of the amido groups, and by synthesis and partial oxidation of the N-free fraction remaining (F. Müller).

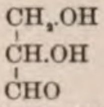
According to a summary of Langstein, the following possibilities are to be considered. Lactic acid can be obtained very easily from alanin by the action of nitrous acid. This is an isomer of glycerin aldehyde which easily condenses to dextrose.


$\begin{array}{l}CH_3\\|\\CH.NH_2\\|\\COOH\end{array}$

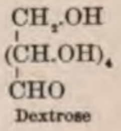
Alanin


$\begin{array}{l}CH_3\\|\\CH.OH\\|\\COOH\end{array}$

Lactic acid


$\begin{array}{l}CH_2.OH\\|\\CH.OH\\|\\CHO\end{array}$

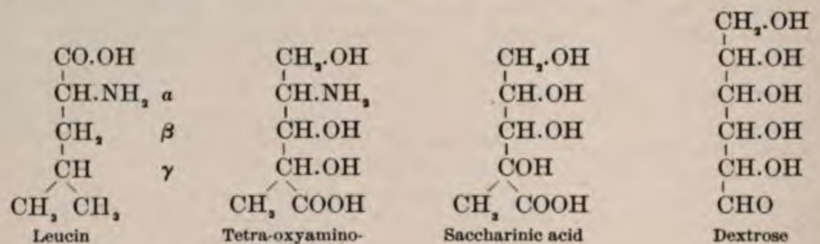
Glycerin aldehyde


$\begin{array}{l}CH_2.OH\\|\\(CH.OH)_4\\|\\CHO\end{array}$

Dextrose

In fact after feeding with alanin lactic acid is observed in the urine, sometimes also an increase of the liver glycogen. Whether we have here a direct or an indirect formation of glycogen (cf. page 126) cannot be decided.

Moreover sugar might be formed from leucin by passing through the stage of tetra-oxyamino-caproic acid (actually demonstrated in the body) to dextrose.



It would be possible also for leucin, by breaking down the carbon chain between the β and γ atoms, to pass into sugar by way of alanin and lactic acid.[1] Observations on diabetic patients likewise favor this idea of a production of sugar from leucin; for by feeding leucin, a distinct increase of the sugar elimination is obtained.

Finally, a production of sugar from diamino acids by way of oxyamino acids is possible.

§ 2. THE DECOMPOSITION OF CARBOHYDRATES

The carbohydrates absorbed from the intestine reach the blood for the most part as dextrose. If the percentage of sugar in the blood by reason of an extra large quantity in the food, exceeds a certain low limit (from 0.2 to 0.3 per cent), a part of the sugar is eliminated through the kidneys in the urine (*alimentary glycosuria*, cf. page 127); otherwise the urine contains only traces of sugar. The kind of sugar appearing in the urine under these conditions is always the same as that fed in excess. Starch does not produce alimentary glycosuria, probably because a sudden flooding of the blood with sugar is prevented by its relatively slow rate of digestion.

Sugar which is not immediately oxidized *is stored in the body either as fat or as glycogen,* and is then drawn upon as required. The greatest part of the glycogen is deposited in the liver, but it is not burned there. It passes in some way into the general circulation and is oxidized in the tissues of the body, especially in the muscles. It is possible that this transportation is accomplished in part by the help of the leucocytes. Another and in all probability a much more important part takes place by the *transformation of glycogen into dextrose,* which is then carried in solution by the blood plasma.

---

[1] This possibility is strengthened by the observation of Embden, Salomon and Schmidt that acetone is obtained by perfusion of leucin through a glycogen-free liver. Quite recently also Lusk and A. R. Mandel have shown that in phloridzin diabetes sarcolactic acid, injected subcutaneously, can be synthesized into dextrose; and Almagia and Embden have obtained a production of lactic acid by perfusing blood containing glycogen or dextrose through a liver containing no glycogen, as well as by perfusing a blood or in sugar through a liver rich in glycogen. Lusk has suggested, therefore, that the ry in the body of carbohydrates derived from proteid may include the following : (1) lactic acid, (2) dextrose, (3) glycogen, (4) dextrose, (5) lactic acid.—ED.

The physiological production of sugar in the liver which was discovered by Cl. Bernard (1853), has since that time often been denied on the assumption that the increase of sugar easily demonstrated in an excised liver, is due to post-mortem processes. This explanation, however, is not borne out by well-authenticated facts obtained from many experiments; hence the formation of sugar in the liver must be regarded as a physiological process.

For example, if a puncture in the middle of the floor of the third ventricle between the points of origin of the auditory nerve and the vagus, be made with a blunt needle, sugar immediately appears in the urine (*puncture diabetes* of Cl. Bernard), and the liver glycogen rapidly disappears. If, however, the puncture experiment be performed on a fasting animal whose liver glycogen is already used up, no sugar appears in the urine.

After a time the liver recovers its ability to store up carbohydrates as glycogen. On this ground the formation of sugar might be regarded as the result of a stimulus, and not as the result of decomposition. The stimulus is conveyed to the liver by the splanchnics, for after section of these nerves the puncture is ineffective.

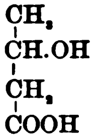
Sugar in the urine can be caused also by stimulation of numerous afferent nerves, as well as by various traumatic and operative effects widely different in character (e. g., concussion or hemorrhage of the brain, inflammation of the brain membranes, neuralgia, etc.). Reflexes are involved here, which, with the coöperation of the medulla, lead to an increased formation of sugar in the liver. By means of these reflexes the working organs, especially the muscles, remove from the liver the carbohydrate fuel required in the performance of their functions. They constitute, therefore, as Pflüger has pointed out, an important regulatory mechanism for the consumption of the available material in the body.

The transformation of glycogen to sugar is regarded by some authors as an expression of the vital activity of the liver cells; others explain it as the effect of a special enzyme which is formed in the cells.

After extirpation of the pancreas (cf. page 362), after poisoning with the glucoside phloridzin, in diabetes mellitus, and under certain other circumstances, the metabolism of the carbohydrates undergoes a chronic change, so that sugar in abnormally large quantities is given off in the urine. In phloridzin poisoning this is caused primarily by an increased permeability of the kidneys to sugar, whereas the other forms of morbid glycosuria arise because the body has lost to a greater or less extent the power either to burn sugar or to store it up as glycogen or fat.

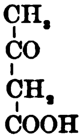
In the so-called light form of diabetes, sugar is given off through the kidneys only in case the food contains carbohydrates; if carbohydrates are prohibited, the loss of sugar ceases. In the severe form of the disease to which pancreatic diabetes belongs, sugar appears in the urine even if no carbohydrates be given in the food. The body then oxidizes little or no sugar, although its power to oxidize is not at all reduced. Since, as was above remarked, at page 128, sugar is probably not formed from fat in the body, the sugar in this case must come from the proteid.

In diabetes there appear in the urine besides sugar the so-called acetone bodies: β-oxybutyric acid, aceto-acetic acid and acetone, the relations of which to each other are evident from the following formulæ:



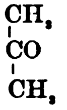
$$\begin{array}{l} CH_3 \\ | \\ CH.OH \\ | \\ CH_2 \\ | \\ COOH \end{array}$$

β-Oxybutyric acid



$$\begin{array}{l} CH_3 \\ | \\ CO \\ | \\ CH_2 \\ | \\ COOH \end{array}$$

Aceto-acetic acid



$$\begin{array}{l} CH_3 \\ | \\ CO \\ | \\ CH_3 \end{array}$$

Acetone (di-methyl-ketone)

With the exception of acetone, which is eliminated in small quantities under physiological conditions also, these compounds never, so far as known, appear in the normal urine; from which it follows that diabetes must be intimately connected with deep-seated changes in the general metabolism.

Most of the carbohydrates pass through the stage of hexoses before they are further decomposed in the body. Like the other foodstuffs they are not immediately oxidized to their end products, but pass through more or less complex groups before being eliminated as carbon dioxide and water. To these intermediary products belong: glycuronic acid $CHO.(CHOH)_4.COOH$, which in its turn can be transformed into oxalic acid in the body; sarcolactic acid (?); and ethyl alcohol. It cannot be decided yet from the observations thus far reported whether sugar always breaks up in the same way, or whether under different circumstances and in different organs it runs through different cleavage products.

§ 3. THE DECOMPOSITION OF FAT

Fat eaten in excess is directly deposited as such in the fat cells. How it is transported and how deposited is not yet entirely clear. Metzner in his investigations of this question was unable to find anywhere a depository where fat was entering cells in corpuscular form; he never found in the immediate neighborhood of cells any fatty granules similar to those found inside of the cells. Moreover, in the very early stages of deposition, fat is not laid down in the form of granules, but in the form of minute vacuoles which expand and enlarge from day to day (cf. page 304). These facts are interpreted by Metzner and Altmann to mean that fat is added to the cells only in the form of soluble cleavage products (fatty acids), which are synthesized again into neutral fats in the cell. It is not unlikely that fat is again split up when it leaves the fat cells and is carried to the different organs in soluble form.

For the purpose of obtaining some light on the oxidation of fats in the animal organism, Pohl has studied the behavior in the body of those intermediary cleavage products which theoretically may be expected to appear in the normal course of fat destruction. Thus, if the series of substances which can be formed in the oxidation of highly complex fatty bodies—i. e., fatty acids and carbohydrates—be arranged in order, it is seen that relatively simple intermediary compounds precede the formation of CO_2, alike for the most widely different bodies. If now it can be shown by experiments on animals that some of the theoretically possible predecessors of carbon dioxide, when injected directly into the animal body, are destructible but others are not, some idea can be formed whether or not such intermediary compounds appear in the physiological oxidation of complex fat bodies. Pohl's investigation has shown, for example, that oxalic acid is indestructible in the animal body; that the acids presumably occurring in the oxidation of the ethane derivatives, glycolic acid, $CH_2.OH.COOH$, and glyoxylic acid, $CH(HO)_2.COOH$, can be destroyed in relatively large quantities without forming any oxalic acid, as occurs when they are oxidized outside the body. Therefore, the most highly oxidized acid of the series, which is combustible in the body, namely glyoxylic acid, may be considered as the stage immediately preceding the carbon dioxide excreted. Glycol, $CH_2OH.CH_2OH$, is only partly combustible in the body without forming oxalic acid. Malonic acid, $CH_2(COOH)_2$, tartronic acid, $CH.OH(COOH)_2$, mesoxalic acid, $(HO)_2.C.(COOH)_2$, glyceric acid, $CH_2.(OH).CH(OH).COOH$, are combustible and thus their production as intermediary stages in animal combustion is rendered possible. On the other hand, the body has the power to burn tartaric acid, $C_4H_6O_6$, only to a slight extent.

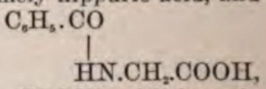
CHAPTER XIII

THE EXCRETIONS OF THE BODY

SEVERAL organs, the skin, the intestine and liver, the lungs and the kidneys, in addition to their other functions have the function of eliminating various substances which are useless or harmful to the body. We place first among these substances the products formed in the decomposition of the foodstuffs. Substances also which enter the body in one way or another, and themselves exert a harmful influence are thrown out either unchanged or more or less transformed by the activity of some organ. These transformations in many cases are for the purpose of *changing harmful substances,* which cannot be eliminated at once, into relatively harmless ones. We have already become acquainted with an example of this in the formation of urea out of ammonium salts (cf. page 370). Here belong also the following phenomena:

In the putrefaction of proteid in the intestine there arise among other products indol, skatol, paracresol, phenol, phenyl-propionic acid, phenyl-acetic acid, paroxy-phenyl-acetic acid, paroxy-phenyl-propionic acid, etc., all belonging to the aromatic series—which in part pass into the circulation. Of these the last two named (the so-called aromatic oxyacids), paroxy-phenyl-propionic acid, $C_6H_4(OH).C_2H_4.COOH$, derived from tyrosin by the splitting off of ammonia, and the oxidation product of this acid, paroxy-phenyl-acetic acid, $C_6H_4(OH).CH_2.COOH$—these two pass out in the urine mostly unchanged. The others are not burned in the body, but before they come out in the urine, they undergo a synthetic transformation by which they are rendered innocuous.

The earliest known example of such transformations is the demonstration by Wöhler (1824) that benzoic acid, when ingested into the animal body, passes over into an acid rich in carbon, but poor in nitrogen, namely hippuric acid, and is excreted as such through the kidneys. Hippuric acid,

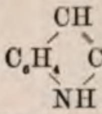
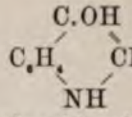
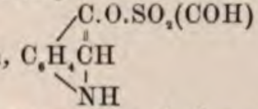


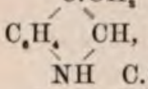
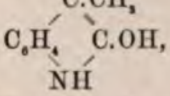
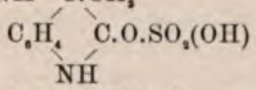
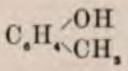
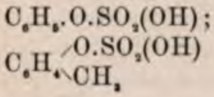
$$\begin{array}{l}C_6H_5.CO\\ \qquad\;|\\ \quad HN.CH_2.COOH,\end{array}$$

is a compound of glycocoll (amino-acetic acid, $NH_2.CH_2.COOH$) with benzoic acid, which is an oxidation product of phenyl-propionic acid ($C_6H_5.CH_2.CH_2.COOH$) formed in intestinal putrefaction.

The synthesis of hippuric acid takes place in the dog exclusively in the kidneys (Schmiedeberg and Bunge), but in the rabbit in other organs also such as the liver and muscles. If salicylic acid, oxybenzoic acid, paroxy-benzoic acid, etc., instead of benzoic acid, be fed to mammals they all undergo transformations analogous to that of benzoic acid into hippuric acid, since like it they unite to a greater or less extent with glycocoll. The acids thus formed have been designated as salicyluric, oxybenzuric, paroxybenzuric, etc.

The following syntheses appear to take place in different organs of the body, especially in the liver:

Indol,  $C_6H_4\begin{matrix}\diagup CH \diagdown\\ \diagdown NH \diagup\end{matrix}CH$ passes after absorption into indoxyl,  $C_6H_4\begin{matrix}\diagup C.OH \diagdown\\ \diagdown NH \diagup\end{matrix}CH$, and this body then unites with sulphuric acid into indoxyl-sulphuric acid, urine indican,  $C_6H_4CH\begin{matrix}\diagup C.O.SO_2(COH)\\ \diagdown NH\end{matrix}$

In an exactly similar way there arise from skatol or methyl-indol,  $C_6H_4\begin{matrix}\diagup C.CH_3 \diagdown\\ \diagdown NH \diagup\end{matrix}CH$, first skatoxyl,  $C_6H_4\begin{matrix}\diagup C.CH_3 \diagdown\\ \diagdown NH \diagup\end{matrix}C.OH$, and then, skatoxyl-sulphuric acid,  $C_6H_4\begin{matrix}\diagup C.CH_3 \diagdown\\ \diagdown NH \diagup\end{matrix}C.O.SO_2(OH)$; from phenol, $C_6H_5.OH$, phenol-sulphuric acid, $C_6H_5.O.SO_2(OH)$; from paracresol,  $C_6H_4\begin{matrix}\diagup OH\\ \diagdown CH_3\end{matrix}$ paracresol-sulphuric acid,  $C_6H_4\begin{matrix}\diagup O.SO_2(OH)\\ \diagdown CH_3\end{matrix}$

If the sulphuric acid available is not sufficient for the combination of the phenols, they are paired with glycuronic acid (page 376). This acid is an intermediary product of metabolism and is further decomposed except when it is protected from combustion by pairing with other substances.

We have already studied the processes of excretion in the intestine, in the liver and in the lungs. There remains for us to discuss excretion through the kidneys and the skin.

FIRST SECTION

THE URINE AND ITS EXCRETION

§ 1. THE URINE

The urine is formed by the action of the kidneys. It contains the most of the nitrogenous and sulphur-containing products of metabolism as well as a large number of other substances to be eliminated from the body.

A. THE GENERAL PROPERTIES OF THE URINE

The reaction of a sample of urine differs according to the indicator used. With phenolphthaleïn it is acid, with litmus acid, neutral or alkaline, with methyl orange, alkaline. This difference is referable to the properties of the different indicators, which, according to the theory worked out by Ostwald, represent weak acids or bases whose radicals as free ions possess other colors than those which the electrically neutral molecules possess. Thus phenolphthaleïn in the nondissociable condition is colorless; as soon however as the solution is rendered alkaline a salt of high dissociability is formed, and the intensely red color of its negative ion comes to the fore. But in order that the reaction may appear with a very slight excess of hydroxyl or hydrogen ions the acid or base used as the indicator must be very weak in comparison to the acid or base to be tested. The acidity of weak acids obviously can only be determined by the help of an indicator which itself is still weaker than the weakest of the acids to be tested; in the presence of weak bases the alkalinity can only be ascertained with the help of a somewhat stronger acid as indicator—e. g., methyl orange.

Now the urine contains weak acids such as CO_2 and H_3PO_4 in considerable quantities and a rather weak base, ammonium, in very small quantities. In order to obtain the true reaction of urine, one must, therefore, use a very weak acid as indicator. Neither methyl orange nor litmus is weak enough to be liberated by carbon dioxide or to detect phosphoric acid as a dibasic, much less as a tribasic acid. Phenolphthalein, however, is sensitive to both, although the third hydrogen atom of phosphoric acid escapes it.

With phenolphthalein the reaction of the urine is always neutral or weakly acid. A plainly alkaline reaction is never met with except in urine which has suffered bacterial decomposition (Auerbach and Friedenthal).

By titration one may ascertain the true chemical acidity of the urine measured as the quantity of alkali which must be added to displace all the acid hydrogen with a metal. From the physico-chemical standpoint, however, acidity means the *concentration of hydrogen ions* present in the liquid. According to v. Rhorer and Hoeber, 1 L. of urine contains on the average about 0.003–0.005 (minimum 0.0004, maximum 0.01) mg. of ionized hydrogen as compared with 0.0001 mg. in distilled water. This acidity corresponds to an acid which in $\frac{n}{10}$ solution is dissociated to $\frac{1}{100}$ per cent, and is some ten thousand times less than that determined by titration.

In view of the very complicated physico-chemical relations of the urine, it is scarcely possible to determine the share of the different constituents in its total acidity.

Fresh urine as a rule is perfectly clear; but on standing it sometimes becomes turbid owing to the separation of urates. There also appears in it a weak flocculent precipitate (nubecula), which, according to K. A. H. Mörner, contains a special mucous substance (urine mucoid), probably formed in the mucous membrane of the urinary passages and mixed with the urine as a weak gelatinous solution.

The *color of the urine* depends to a certain extent upon its concentration, and varies with increasing concentration from straw yellow to dark reddish yellow and reddish brown. Its taste is salty, its odor peculiarly aromatic.

The *quantity* of urine depends upon many circumstances, and therefore varies considerably. The average quantity for an adult man may be estimated at about 1,500 c.c. per day.

The *specific gravity* of the urine also varies in man from 1.017 to 1.020; but it may fall as low as 1.002 and rise as high as 1.047.

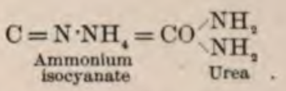
The molecular concentration (Δ) of the urine, measured by the lowering of the freezing point, stands in a certain relation to the specific gravity (s), and can be estimated approximately by the formula: $\Delta = 75\ (s-1)$. The relation between the molecular concentration of organic (Co) and inorganic (Ci) molecules, $\frac{Co}{Ci}$, is commonly 0.75 (Burgarsky).

Urine injected intravenously into an animal produces an acute poisoning which results fatally. The toxicity of different urines appears to be somewhat different, and Bouchard designates as the toxic unit (urotoxy), the quantity (cubic centimeters per kilogram) of urine sufficient to kill a rabbit: this quantity varies from 30–60 c.c. According to Beck, the toxicity of normal urine depends upon the presence of potassium salts; however, there are alkaloidal substances in the urine which are present only in small quantities normally, but under abnormal conditions are probably eliminated in larger quantities, and these might therefore increase its toxicity.

B. COMPOSITION OF URINE

1. *Urea*, or carbamide (cf. page 370; also Fig. 139), is the most important and most abundant constituent of urine. The daily excretion depends upon the supply of proteid in the food. On Voit's normal ration for a moderate worker, the quantity is about 30 g. per day. Usually two to three per cent of the urine is urea. About ninety per cent of the total quantity of nitrogen in the urine of man appears in the form of urea.

Urea was first separated from urine by Rouelle (1773). In 1828 Wöhler succeeded in preparing it synthetically by heating a solution of ammonium isocyanate:



$$\underset{\text{Ammonium isocyanate}}{C{=}N{\cdot}NH_4} = \underset{\text{Urea}}{CO\begin{matrix}\diagup NH_2\\ \diagdown NH_2\end{matrix}}\ .$$

This synthesis was the first instance of the production by artificial means of a substance occurring in the animal body, and led the way for all the organic syntheses possible to modern science. For this reason Berzelius proposed that the radical of urea be named proïn (signifying "dawn").

The origin of urea in the animal body has already been considered in Chapter XII. Here we may add the following data from Schöndorff with regard to the percentage of urea in the different organs. These relate to a dog of 32 kg. weight after abundant meat feeding. The organs investigated amounted altogether to fifty-three per cent of the entire body.

ORGAN.	Per cent of urea.	Absolute quantity in gms.
Blood	0.116	1.36
Muscle	0.080	12.15
Liver	0.112	0.94
Kidneys	0.670	1.04
Heart	0.173	0.29
Spleen	0.122	0.12
Pancreas	0.119	0.06
Brain	0.128	0.92
Total		16.88

The percentage of urea in the individual organs, with the exception of the muscles, the heart and the kidneys, is thus about the same as that of the blood—i. e., on the average 0.12 per cent. The high percentage in the kidneys is to be explained by the presence there of urea formed in other organs, and which is necessarily included in making the analysis.

2. *Oxyproteïc acid* was discovered by Bondzynski and Gottlieb (1897). Its barium salt, according to the analyses of various authors, has the following composition: C 27.5–30.0, H 3.9–4.1, N 7.0–10.6, S 1.6–1.8, Ba 28.7–29.8, O 26.5–31.6. The quantity of this acid (calculated as the Ba salt) excreted in twenty-four hours amounts to not less than 3–4 g.

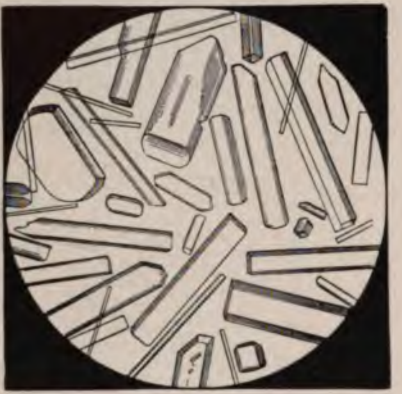


FIG. 139.

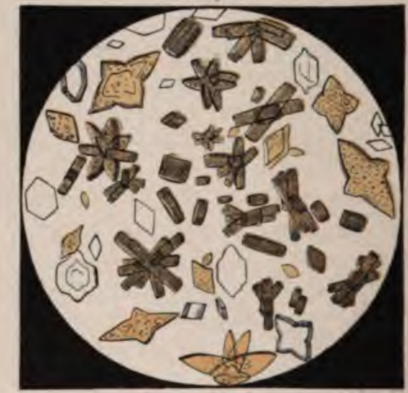
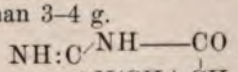


FIG. 140.

FIG. 139.—Crystals of urea, obtained from human urine after long-continued evaporation, after Funke.

FIG. 140.—Crystals of uric acid, after Funke. Some of the forms represented were obtained by solution and recrystallization of chemically pure uric acid; some by treatment of urinary sediments containing urates with mineral acids; some by spontaneous crystallization from urine. Most of the crystals are tinged with urea.

3. *Creatinin,* Methyl-glyco-cyanamid,  $\mathrm{NH{:}C}\begin{array}{l}\diagup\mathrm{NH}\text{——}\mathrm{CO}\\ \diagdown\mathrm{N(CH_3).CH}\end{array}$ occurs to the extent of about 0.25 per cent in the urine. The daily output in the urine amounts to 0.6–2.1 g. and may be estimated at 1 g. as a mean value.

4. *Ammonia,* NH_3. The daily quantity amounts to 0.5–0.9 g. = two to four per cent of the nitrogen in the urine. The ratio of ammonia to urea is approximately 1 : 40 (cf. page 371).

5. *Uric acid* (Figs. 140 and 141) 2, 6, 8-tri-oxypurin (page 373) occurs in the urine of man and the mammals only in small quantities (about 0.7 g. per day). This is a dibasic acid. Of the alkaline urates, the neutral potassium and lithium salts are the most soluble, the acid ammonium salt least so; the urates of the alkaline earths are also very difficultly soluble. In the urine, uric acid probably occurs as monosodium urate which is held in solution mainly by disodium phosphate.

6. Uric acid is derived from the *purin bases* and is in its turn oxidized to *allantoïn* (cf. page 373). These substances also occur in the urine: the purin bases to the extent of 0.08–0.13 g. (mean).

Of the total organic substance in the urine, urea, creatinin, ammonia, uric acid and purin bases together constitute seventy-five per cent, but they contain ninety-three per cent of the total nitrogen of the urine (Donzé and Lambling).

7. *Oxalic acid* occurs in very slight traces.

8. *Hippuric acid* (Fig. 142), benzoyl-glycocoll (page 378) occurs in considerable quantity in the urine of herbivorous animals and in smaller quantity in the urine of man. In the latter on ordinary diet it amounts to only about 0.7 g. per day; after a plentiful quantity of vegetable foods it may reach 2 g. or more per day.

9. The *ethereal sulphates* and the aromatic oxyacids already mentioned at page 379. The quantity of the former per day in the urine of man is only about 0.09–0.62 g.; the oxyacids amount to about 0.03 per day.

10. Among the *pigments* of the urine the iron-free, nitrogenous *urochrome*, carefully studied by Garrod, is the most important. Besides, there are present in normal urine: the red pigment *uroerythrin, hæmatoporphyrin* (in very small quantities), and *urobilin*, first described by Jaffé. The latter has a red or reddish-yellow color, and in the opinion of many authors is identical with hydrobilirubin ($C_{32}H_{40}N_4O_7$); but this is contested by others on the ground that hydrobilirubin contains twice as much nitrogen as urobilin. *Sterkobilin* (cf. page 295), on the other hand, has exactly the same composition as urobilin. At all events urobilin, as well as other pigments, probably stands in a close relationship both to the bile pigments and to the blood pigments.

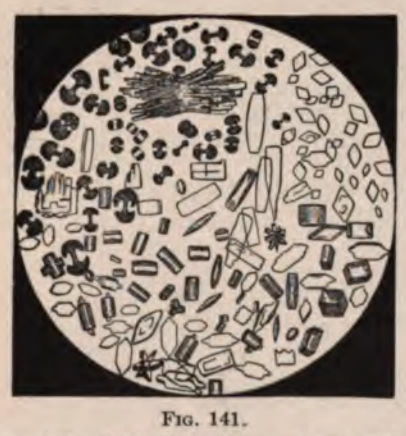


Fig. 141.

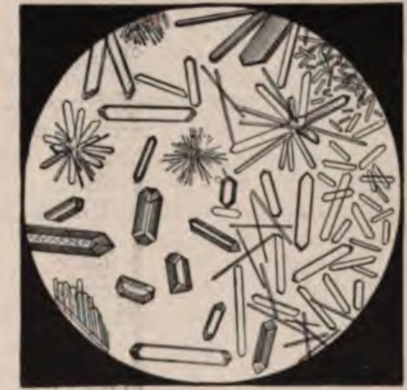


Fig. 142.

Fig. 141.—Still other forms of uric-acid crystals, after Funke. The "wheat stone" and "sheaf" crystals especially are shown. Some of them were found ready formed in urinary sediments; others were obtained by treatment of ordinary sediments containing sodium urate with acids.

Fig. 142.—Hippuric-acid crystals, obtained from human urine by recrystallization from a water solution, after Funke.

11. The urine contains also under perfectly normal circumstances *reducing substances* and *proteids*, though in very small quantities.

Besides uric acid and creatinin, the reducing substances are dextrose, isomaltose (?), animal gum, and conjugated compounds of glycuronic acid (page

376. The reducing power of normal urine corresponds to a 0.15–0.6-per-cent solution of dextrose.

Heller's test (cf. page 69) is commonly used to demonstrate proteid in the urine. A urine which does not give this reaction is generally regarded as free of proteid. And yet there is proteid, chiefly serum albumin, even in such urine.

12. The *inorganic constituents* of the urine on a normal diet amount to about 25 g. per day. For the most part they come from the ingested food, and consequently decrease in fasting. Naturally their percentages vary greatly; hence the following table is only for the purpose of giving a general idea of the average quantities:

Sodium chloride, NaCl	15.0 g.	per day
Sulphuric acid, H_2SO_4	2.5 g.	"
Phosphoric acid, P_2O_5	2.5 g.	"
Potassium, K_2O	3.3 g.	"
Magnesium, MgO	0.5 g.	"
Calcium, CaO	0.3 g.	"
Other inorganic substances	0.2 g.	"

Besides these the urine contains 4–5 vols. per cent of CO_2 which for the most part is physically absorbed, but occurs also in the form of acid carbonates.

13. *Accidental constituents.* The urine may contain either in solution or suspension a large number of different bodies coming from substances ingested for one reason or another, or originating from abnormal processes in the body. I shall merely enumerate the most important of these:

(*a*) Blood, blood pigments and their derivatives; blood corpuscles, hæmoglobin, methæmoglobin, hæmatin, melanin, etc.

(*b*) Bile acids, bile pigments, and their transformed products.

(*c*) Leucin, tyrosin, and dioxy-phenyl-acetic acid, $C_6H_3(OH)_2 \cdot CH_2 \cdot COOH$.

(*d*) Proteid.

(*e*) Sugar.

(*f*) Acetic acid, β-oxybutyric acid and acetone.

(*g*) Drugs, either as such or as transformed products.

§ 2. THE EXCRETION OF URINE

In no other secreting organ are the peculiarities of structure so significant for a conception of its function as in the kidney. It is therefore necessary to discuss the microscopic structure of the kidney here somewhat in detail.

A. STRUCTURE OF THE KIDNEYS

The larger branches of the *renal artery* (Fig. 143) run along the outer surface of the pyramids to their base and there form an anastomosing network. From this network branches pass toward the surface of the kidney (radial arteries), and others pass off in tufts toward the pelvis of the kidney. The individual branches of the latter run between bundles of urinary tubules in the pyramids.

The *radial arteries* send out small branches, *vasa afferentia*, which soon break up in the so-called glomeruli of the Malpighian corpuscles presently to be described. From these, a new vessel, the *vas efferens*, arises and this in its turn breaks up into a capillary network which embraces the kidney tubules. Those *vasa efferentia* which belong to the deeper layers of the cortex push down into the outer layer of the medulla, and from here run between the renal tubules and break up into tufts of vessels, whence again proceed capillaries to the tubules.

From the capillaries of the renal cortex the blood collects in venous trunks which run parallel with the radial arteries to the outer layer of the medulla, and like them form an anastomosing network at the base of the pyramids. Into this network empty the veins from the medullary substance, which, like the arteries, run in the interstices between the renal tubules and converge forming tufted groups.

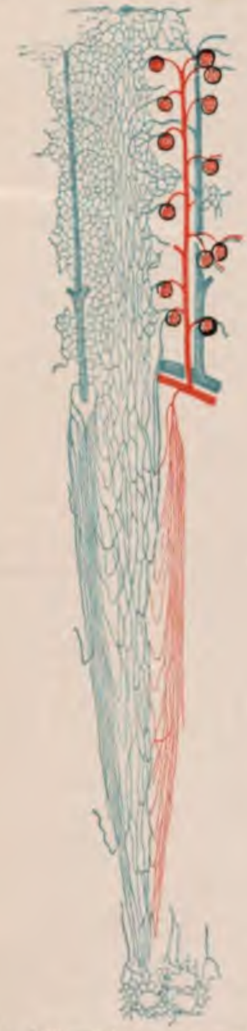


FIG. 143.—Schema representing the distribution of the blood vessels of the kidney, after Ludwig. Arteries red, veins blue.

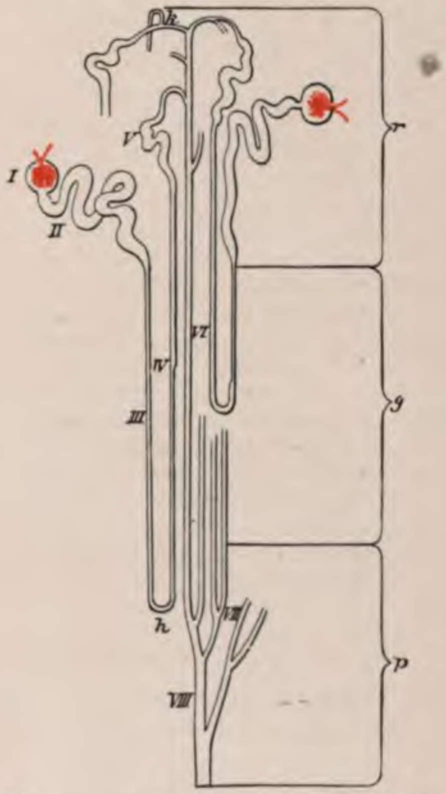


FIG. 144.—Schematic representations of the secreting and conducting elements of the kidney, after Ludwig. *I*, Bowman's capsule; *II*, first convoluted tubule; *III*, *IV*, Henle's loop; *V*, second convoluted tubule; *VI*, collecting tubule; *r*, cortex; *g*, medulla; *p*, papilla.

The *glomerulus* interpolated between the *vas afferens* and the *vas efferens* has the following structure. The afferent arteriole breaks up into several branches, each of which by repeated division forms a lobule composed of several collateral vessels. These vessels do not anastomose, but unite finally to form a simple *vas efferens*, the beginning of which lies in the middle of the glomerulus. They have a simple wall and hence are to be regarded as capillaries. In the kidney therefore the blood passes through *two sets of capillaries*, one in the glomeruli and the other between the secreting elements.

The *secreting* and *conducting elements* of the kidney are numerous, much-convoluted tubules, which begin at the glomeruli and end on the free surface of the papillæ. The glomerulus is surrounded by a thin capsule (the capsule of Bowman), the whole constituting a Malpighian corpuscle (Fig. 144, I). The capsule is a vesicle composed of thin epithelial cells of 0.13 to 0.22 mm. diameter, and, like the serous sacs, consists of two layers, a visceral and a parietal. The former layer is closely applied to the surface of the glomerulus and is reflected at the place where the vessels enter the glomerulus to form the latter layer. From the point opposite the entrance of the vessels the capsule is continued into the *renal tubule*. In the transition to this there comes first a short, narrow neck; then follows a much *convoluted portion* (II) 0.045 mm. in diameter which reaches down to and enters the outer layer of the medullary substance. Here the tubule suddenly diminishes in size very considerably (the diameter is only 0.014 mm.) and passes into the medullary substance, then turns back, forming a *loop* (loop of Henle, III and IV) and runs toward the cortex. Sooner or later it becomes enlarged (0.026 mm.) and soon thereafter becomes convoluted again (V). Then it unites by means of a narrow *connecting portion* with a collecting tubule (VI).

Up to this point each tubule is independent of every other, forming no anastomoses. The collecting tubes, however, in their course through the medullary substance, unite repeatedly with others, so that finally the number of tubes opening on the surface of a papilla is only about fourteen to twenty, whereas there are from 4,000 to 6,000 collecting tubules tributary to them.

The *epithelium* of the urinary tubule and of the collecting tubule is different in different divisions. In the human fœtus Bowman's capsule is composed of cubical cells; in the newborn child the cells are flatter, and later they become very thin. The convoluted tubules, the thicker portion of Henle's loop, and the collecting tubule are lined with fairly tall epithelial cells, which present minor differences in the different divisions named. In the narrower portion of Henle's loop the epithelium consists of clear, flat, spindle-shaped cells.

B. MECHANISM OF THE EXCRETION OF URINE

Any attempt to explain theoretically the process of secretion in the kidneys must take into account the remarkable arrangement of its blood vessels and the renal tubules.

In the glomeruli the blood flowing in is suddenly divided into a considerable number of tiny streams, which of course must favor the passage of constituents into the capsule. Moreover, the *vas efferens* has a smaller diameter than the vas afferens, and it is divided up within a short space into another true capillary network. The *resistance* distal to the glomeruli must therefore be much greater than the resistance proximal to them, which means that the blood must flow through the glomeruli under a relatively high pressure. If now the further fact that the renal tubules begin with the Bowman's capsule surrounding the glomeruli be considered, it cannot readily be denied that, seen merely from the anatomical point of view, the glomerulus and the capsule must play an extremely important part in the secretion of urine. A theoretical account of the kidney function must assign some purpose also for the tortuous course of the tubules up to the point where they enter the collecting tubules.

This has been done in the view advanced by Ludwig and supported by many experiments, namely that a *process of filtration* takes place from the glomerulus into the capsule, and that the filtrate represents a very dilute urine, which during its passage through the tubules *becomes gradually concentrated* by transfusion of water into the lymph bathing their outer surface.

To test this view we have first of all to form some conception of the physico-chemical processes necessary for the filtration of liquid through the capsular epithelium. As Tammann was the first to show, the latter cannot be regarded as a semipermeable membrane, for, if it were, a blood pressure sufficient to overcome the osmotic pressure of the plasma—several atmospheres—would be required to force the filtrate through. On this account Tammann considers the epithelium completely permeable to all the crystalloids dissolved in the urine, and impermeable only to the colloids. In order to separate a proteid-free filtrate of the composition of the crystalloids found in the plasma, the blood pressure need only be high enough to overcome the osmotic pressure of the colloids occurring there. The latter according to Starling amounts to about 25–30 mm. Hg.

However, the osmotic pressure of the sugar in the blood (more than 100 mm. Hg.) is not taken into account in this calculation; whereas it may be considered that the capsular epithelium is permeable to sugar just as to the other crystalloids. It is possible too that the sugar is not free, but occurs in the blood in chemical composition with other substances such as lecithin or proteid. If this were true the osmotic pressure occasioned by the sugar would of course be considerably lower than if it were dissolved as such in the plasma.

The lowest pressure in the glomeruli at which a production of urine could take place would thus be about 25–30 mm. Hg. And yet Gottlieb and Magnus have shown that under the influence of diuretic substances, separation of urine can take place with a carotid pressure of only 6–9 mm. Hg.

Besides this difficulty we have another just as little to be explained from the standpoint of the filtration hypothesis, and that is this: if the supply of the blood to the kidney be completely interrupted by clamping the renal artery for a short time, say one and one-half minutes, the formation of urine stops and is resumed again only after a considerable time (as much as forty-five minutes). The properties of a perfectly inert filter could scarcely be changed to such an extent by anæmia of so short a duration.

The second part of Ludwig's theory likewise meets with several difficulties. If the glomerular filtrate as above assumed has the same composition and therefore the same osmotic pressure as the blood plasma (with the exception of the colloids) then only the osmotic pressure occasioned by the colloids can have anything to do with the concentration of the filtrate. Whether or not this force is sufficient to produce the necessary transfusion of water back into the lymph has not yet been decided. Moreover, the proportion of crystalloids in the urine is quite different from that in the blood. It requires more than the mere absorption of water to get a fluid with the properties of the urine out of such a filtrate as we are able to suppose this to be; we must assume an unequal absorption of different constituents. Finally, it would be impossible for this fluid to be absorbed back into the lymph by purely osmotic processes, for the osmotic pressure of the urine as a rule is higher than that of the blood plasma.

For these and other reasons those authors who regard the process in the glomeruli as a pure filtration are themselves inclined to explain the reabsorption from the urinary tubules postulated by this theory, as an active process carried on in virtue of the vital properties of the parenchyma cells. By so doing, however, the fundamental position of Ludwig's theory is surrendered, for that theory set out to give a purely physico-chemical explanation of the secretion of urine, without reference to vital processes.

But can it be regarded as proved that a reabsorption of fluid passed through the capsule actually takes place in the urinary tubules? Is it not possible that we have here not an absorptive but a *secretory process?*

In order to answer this question Heidenhain carried out some experiments on the elimination of sodium indigosulphate, which is easily recognized in microscopical preparations, and reached the conclusion that this salt is thrown out by the epithelium of the urinary tubules. From analogy he concluded that the same is true of urea and other specific constituents of the urine, and that therefore the tubules have the function of enriching the fluid coming from the capsule with solid constituents.

Direct observations on the elimination of urea are not feasible because there are no micro-chemical reactions by which urea can be recognized. But in birds and reptiles it is not a difficult matter to demonstrate uric acid microscopically. And yet investigators of the subject have not succeeded in satisfactorily demonstrating uric acid within the epithelial cells. Hence, the mode of separation of sodium indigosulphate cannot be regarded as determinative for the elimination of the normal constituents of the urine. Moreover, the microscopical findings after injection of dyes are not harmonious, for the pictures obtained have been regarded by other authors, like v. Sobieranski, as the indication of an absorptive process going on in the urinary tubules.

The following experimental fact speaks strongly for secretion by the epithelium of the urinary tubules. The frog's kidney receives its blood vessels partly from the renal artery, partly from the renal-portal vein. The former provides the glomerulus, the latter the tubules. As was remarked by Nussbaum, and later verified by Beddard, the glomeruli or the urinary tubules can be thrown out by tying off the one or the other of these vessels. After tying the renal artery the flow of urine ceases entirely. If the fluid coming through the capsule of Bowman during its passage along the tubule were to become thicker by absorption of water, then tying the renal portal ought to produce an increased flow of urine. But according to Gurewitsch this is not true; instead, the quantity of urine is reduced by the operation.

If this observation proves to be absolutely correct, it constitutes a conclusive argument against the doctrine of absorption in the renal tubules. Accordingly, the epithelium would have the function of taking up the specific constituents of the urine from the blood and of delivering them to the urinary tubules.

We come therefore for the present to the following view, first expressed by Bowman and further elaborated by Heidenhain, concerning the activity of the kidneys. *The cells covering the glomerulus give out water and salts by a true process of secretion, those of the convoluted tubules and of* *the wide part of Henle's loop secrete the specific constituents of the urine and water.*

As an indirect support of this theory, the following consequence of the filtration hypothesis, emphasized by Heidenhain, is to be considered. If the outflow of fluid from the glomeruli takes place by filtration, the filtrate cannot be richer in urea than the blood; it would contain therefore about 0.05 per cent urea. Since however the urine as voided contains two per cent of urea, the filtrate must be concentrated forty times. With a daily excretion of 1,500 g. urine containing 30 g. urea the total quantity of filtrate would thus amount to 60,000 g. of which 58,500 g. would have to be absorbed again into the urinary tubules.

Various other circumstances favor the idea of a secretory process in the kidneys. (1) The excretion of urine occasions a measurable rise of temperature (the temperature of the urine may be 0.4° C. higher than that of the blood) (Grijns). (2) Atropin which is poisonous for all glands reduces the excretion of urine to a considerable extent (Thompson), although pilocarpine which is stimulating for glands in general has no effect on the activity of the kidneys (Loewi). (3) When by feeding benzoic acid and glycocoll the kidneys are called upon to synthesize hippuric acid (cf. page 378), the output of NaCl in the urine is considerably increased, notwithstanding that the flow of blood and the percentage composition of NaCl in it remain constant (Asher).

The amount of work done by the kidneys depends essentially on two factors, namely, the *volume of the blood* flowing through them, and the *percentage of diuretic substances* in the blood.

The influence of the blood flow was first established by Ludwig and his pupils on the basis of a great many experimental observations. Everything which increases the blood flow, such as great but not excessive distention of the vascular system, extensive vasoconstriction with the renal nerves cut, etc., intensifies the secretion of urine. Conversely it falls *pari passu* with the blood flow, whether that fall be occasioned by diminution of the general blood pressure due to stimulation of the vagus, to bleeding, to section of the spinal cord, or be caused by a local constriction or compression of the renal vessels.

Since every change of the arterial blood supply alters the pressure in the capillaries in the same direction, the above-mentioned facts were adduced as the most important support for the filtration hypothesis; for it is evident that filtration through the glomeruli should be more abundant, the higher the pressure brought to bear on them. Likewise if the excretion of urine be the result of a secretory process, the *variations of the blood flow are of vast importance*, for by this means the activity of the kidney cells can be influenced in one way or the other.

The *action of diuretic substances* is shown most clearly by experiments on the secretion of urine with the renal veins compressed. It is well known also that the kidney is surrounded by a tolerably firm capsule, and that its mass is incompressible. Here, as in the brain (cf. page 241), venous stasis must, therefore, cause an arterial anæmia. Consequently when the renal vein or inferior *vena cava* is constricted, the secretion of urine declines or stops altogether. If, however, a solution of sodium nitrate, for example, be then injected into the blood, the urine gushes out in a strong stream, even if the general blood pressure be low (Paneth). It is evident that the same effect can be produced with the renal circulation unobstructed.

To the diuretic substances belong: urea, common salt, sodium nitrate, caffein, grape sugar, peptone, albumoses, etc. Their effect undoubtedly depends in part upon the accompanying dilatation of the renal vessels; but it is connected also with a rise in the osmotic pressure of the blood occasioned by these substances, and the consequent abstraction of water from the tissue spaces into the blood vessels. In this way the blood is diluted, and the vessels are more tensely filled; the result being a more copious flow of blood through the kidneys. Here we have almost the same process as when water is slowly transfused into a vein after a certain quantity has been injected; the excretion of urine increases up to a certain point, beyond which the transfusion and excretion keep pace with each other.

The effects of diuretic substances cannot, however, be explained from this point of view alone. For there are various experimental facts which indicate that the ingested substance stimulates the kidneys to increased activity, quite independently of changes in the diameter of the blood vessels, etc., and that, therefore, these substances are specific stimuli for the kidney cells.

Finally, the *general condition of the body* plays a part in the secretion of the urine which is not to be neglected. When certain diuretics are given to a body poor in sodium chloride, there is no increase in the excretion of NaCl. Notwithstanding the diuresis, the body holds on to its NaCl very energetically, giving it up only in the smallest possible quantities. But in cases where the body has plenty of NaCl, whenever there is a strong secretion of urine, there is also an abundant output of this salt.

It has long been known that one kidney is sufficient for all purposes of metabolism. One can even remove as much as two-thirds of the kidney substance and still leave an efficient excretory apparatus. Here moreover we meet the remarkable fact that the renal secretion increases considerably and permanently. At the same time the elimination of urea is increased and animals die within two to six weeks in spite of a fairly good appetite (Bradford). How this phenomenon is to be explained or what theoretical weight it has, we are not able to say at present.

Nothing is known which would indicate the presence of *secretory nerves* to the kidneys. It is true that by various operations on the central nervous system or on peripheral nerves, changes in the secretion of urine may be obtained; but all these admit of an explanation as vasomotor effects. The secretion continues also, though somewhat diminished, after division of the nerves running along the renal vessels. So far, then, as we are able to judge at present, the secretion of urine is accomplished by the influence of the urine-producing substance in the blood, and is regulated by variations in the quantity and the quality of these substances, as well as by alterations in the blood supply to the kidney.

§ 3. MICTURITION

From the pelvis of the kidney the urine flows through the ureters into the bladder, remains there for a time, and is finally expelled at varying intervals.

§ 2. EXCRETION OF SWEAT

A. COMPOSITION AND PROPERTIES

Sweat is the thinnest of all the body fluids, and, when filtered, is clear and colorless, and has a specific gravity of 1.003–1.008. Its reaction to litmus may be acid, neutral or alkaline; its taste is salty; its odor is unpleasant and differs for the different portions of the body. The odor is destroyed by heating it up to 110° C.

In the following table two analyses of sweat are given. The one by Harnack is taken from the sweat of a rheumatic patient, secreted in one to two hours in a vapor bath; the other by Camerer, Jr., was taken from sweat secreted in an electric-light bath in the course of seventy-five to ninety minutes.

	Harnack.	Camerer, Jr.
Water	99.09–99.16 per cent.	97.9 per cent.
Solids	0.91– 0.85 "	2.1 "
Organic matter	0.24– 0.20 "	1.06 "
Inorganic matter	0.67– 0.65 "	1.04 "
NaCl	0.52 "	0.66 "
Phosphates of the alkaline earths	0.03 "	....
H_2SO_4	0.05– 0.06 "	....
KHO	0.05– 0.04 "	....
Urea	0.12 "	0.05 per cent.
Nitrogen	....	0.19– 0.15 "

Human sweat is said to contain also about 0.045 per cent proteid matter and two enzymes, one diastatic and the other proteolytic, as well as ethereal sulphates, aromatic oxyacids, skatol and creatinin in small quantities.

According to Arloing, the sweat of a healthy man possesses toxic properties; by intravenous injection of a dose of 10–15 c.c. per kg. of body weight, it kills a dog in fifteen to eighty-four hours. The sweat produced in work is more poisonous than that given off during a vapor bath. Vomiting and congestion of the alimentary canal are mentioned as the most prominent symptoms. Participation of Bacteria in these phenomena appears to be excluded, because sweat is said to lose only a little of its toxicity by sterilization in the autoclave.

It has long been known that animals, in which the cutaneous secretions are stopped by means of varnishes, die within a short time; and attempts were made to explain this effect by the retention of products normally given off in the sweat. Then came the conviction that the sweat does not remove any toxic substances from the body, and the influence of the varnish was sought in the great radiation of heat caused by it. It is altogether possible that the increased loss of heat has a certain, probably even a great, significance. But if the above-mentioned experimental facts with reference to the toxicity of sweat are confirmed, we must again ascribe the most important rôle to the retention of decomposition products. This view is supported moreover by the fact that varnished animals take only a little food, notwithstanding great loss of heat and the increased heat production thereby demanded—

which has induced Loulanié to describe the death of these animals as death by inanition.

The *quantity of sweat* excreted daily is variable. It depends chiefly upon the requirements of heat regulation. The greater the quantity of sweat secreted, the greater is the absolute quantity of solid constituents, among which urea is of special importance. Ordinarily the output of urea in the sweat is negligibly small, and yet as already observed (page 89), under certain circumstances it may become considerable.

B. THE EXCRETORY PROCESS

In view of the importance of sweat in regulating the temperature of the body, it is but natural to assume that the action of the sweat glands is under the control of the central nervous system. This is confirmed by experiment.

Stimulation of the cut sciatic nerve or of the brachial plexus in a cat produces in a short time large drops of sweat on the balls of the foot (Goltz). This production of sweat is an actual secretion and not a filtration from the blood, for: (1) a powerful secretion can be evoked by stimulation as much as twenty minutes after amputation of a leg (Kendall and Luchsinger); (2) secretion occurs when the pressure of the surrounding air is higher than that of the aortic blood (Levy-Dorn); (3) it does not occur without stimulation when a paw is subjected to a low air pressure; and (4) it is prevented by very small doses of atropine, despite the strongest nerve stimulus.

The *sweat fibers* for the fore paw of the cat have been found in the median and ulnar nerves, for the hind paw in the sciatic. It appears however that most of them do not come directly from the spinal roots of these nerves, but that they first traverse the sympathetic paths (thoracic or abdominal trunk) before they join the nerves to the extremities. The sources of the sweat fibers in the abdominal sympathetic are the three lower thoracic and the four upper lumbar roots; those of the fore paw spring from the fourth thoracic root.

Sweat centers are present in the spinal cord; for if the cord of a young cat be cut at the level of the fourth thoracic root, secretion can be obtained on the hind paws by the influence either of heat or of dyspnœa. Considering the importance of sweat in heat regulation, it is very probable that a general sweat center is present in the medulla, although we know nothing definite about it at this time.

Secretion of sweat is induced by psychical stimuli (fear, etc.), by heat, asphyxiation, and reflex effects, as well as by various poisons. Among the latter, pilocarpine is especially worthy of mention, for it has the power to produce sweat even when the secretory nerves are cut.

The effectiveness of a stimulus applied to the secretory nerves depends mainly upon the temperature of the glands. When very cold, no effect at all is produced, although at a body temperature of 22°–28° C. the glands of a cat's foot can be made to secrete by psychic excitation, by reflex action or by asphyxiation. On the other hand heat produces secretion of sweat even in case the spinal cord is severed at the ninth thoracic root and all the posterior roots of the severed cord are cut—i. e., heat, like asphyxiation, has a direct stimulating effect upon the sweat centers.

Various experimental facts favor the view that sweat glands are under the influence of *inhibitory nerves*, which, like the secretory fibers, traverse sympathetic paths.

Many animals do not sweat at all; others, like the cat, sweat only in certain places, as the balls of the feet. In man the ability to sweat is very highly developed: in varying degrees it is a function of the entire skin—principal places being the brow, palms of the hands and the soles of the feet.

§ 3. THE SO-CALLED INSENSIBLE PERSPIRATION

We include under this head the excretion of carbon dioxide through the skin, and the exhalation of water independently of the sweat glands.

The *elimination of carbon dioxide* through the skin is very small in comparison with the elimination through the lungs. Both this and the exhalation of water vapor have repeatedly been studied on limited areas of the skin; but such investigations, although they may yield valuable results as to the influence of different factors, give no certain criteria for the estimation of the total output of CO_2 and water vapor for the whole surface of the body. In order to make such a determination, an individual is inclosed, all but his head, in a cabinet suitably ventilated, so that the elimination may go on continuously.

According to Schierbeck and v. Willebrand, the output of CO_2 at a temperature of 20°–33° C. is fairly constant, and amounts to 0.35 g. per hour—i. e., 7.2–8.4 g. per day. If the surrounding temperature be raised above 33° C., the output of CO_2 suddenly increases, so that at 33.5°–34° C. it reaches the relatively high value of 0.87–1.35 g. per hour (= 20.9–32.4 g. per day).

This sudden rise is coincident with the appearance of "sensible perspiration"; it is possible, therefore, that it may be due to the increased work of the sweat glands.

Excretion of water vapor goes on also below this critical temperature. Other conditions being equal, it is greater the higher is the surrounding temperature, and from 12°–31° C. the output from the naked body, according to v. Willebrand, is proportional to the atmospheric temperature (e. g., at 12°, 10.5 g. per hour; at 18.2°, 18.4 g.; at 24°, 22.7 g.; and at 28°, 27.3 g.), but with the appearance of visible sweat it rises suddenly.

We can think of two possibilities as to the source of the water given off from the skin before the appearance of sweat: either it is a product of the sweat glands, or it is derived by a purely physical process of diffusion from the gland cells and the epidermis. Considering the proportional increase parallel with the temperature up to the point where water is poured out as visible sweat, the latter possibility seems the more likely.

CHAPTER XIV

ANIMAL HEAT AND ITS REGULATION

§ 1. THE TEMPERATURE OF THE HUMAN BODY

Birds and Mammals differ from all other living creatures in that their body temperature remains constant in spite of all variations in the temperature of the surrounding medium. For this reason they are called *homoiothermous,* or, since the temperature of the medium in which they live is generally lower than their body temperature, *warm-blooded animals.*

Among different species of warm-blooded animals the body temperature exhibits considerable differences. In general it is higher in birds (39.4°–43.9° C.) than in mammals (35.5°–40.5° C.), and among the latter many genera have a higher temperature than that of man, 37.5° C. With a temperature as high as the normal in birds, or even as high as the normal in some other mammals, a man would be very ill.

The temperature of an animal is usually taken in the rectum, that of man either in the rectum or in the mouth or in the axilla. It is evident that the thermometer must always remain in place for a certain length of time if it is to register the temperature exactly; also that the temperature cannot be the same in these different places owing to loss of heat from the superficial parts of the body; and further that of the places named the temperature is highest in the rectum, lowest in the axilla. If the person is doing physical work the temperature in the mouth may fall, whereas the temperature in the rectum rises. This circumstance, which shows that the registration of temperature in the mouth does not always give trustworthy results, is probably due to the cooling of the skin of the face through the agency of sweat, to the augmented respiration by which the lining of the mouth is cooled, etc. (Pembrey and Nicol).

In taking the rectal temperature it is necessary that the thermometer be inserted to a sufficient depth to register the actual temperature of the interior of the body. In the mouth the thermometer bulb is placed under the tongue and the mouth is closed. The posterior opening of the mouth cavity (see page 279) normally is always closed. The axilla never forms a completely closed cavity, but for the purpose of taking the temperature, can be approximately closed by pressing the arm firmly against the chest wall. It requires, however, some time for the temperature in such a cavity to reach its maximum, and hence the thermometer must remain longer in the axilla than in the mouth or in the rectum.

The temperature of the surface, especially of the parts habitually exposed, varies greatly, but for the clothed parts can be estimated in general at

33°–35° C.; the naked skin in a bath of 5° C. still has a temperature of 17°, and in a bath of 18° and 25° has a temperature of 22° and 26.5° respectively. The temperature 2 mm. below the surface—i. e., in the subcutaneous tissues—under the same circumstances is 24°, 24.8°, and 27.5° respectively, and in the muscles 12 mm. below the surface is 36.3°, 35.9°, and 36.9° C. (Lefevre). The organs in the upper part of the abdominal cavity are still warmer than the muscles and the rectum. According to Quincke, the temperature in the interior of the stomach (man) is 0.12° C. higher than the rectal temperature, and according to Ito, that of the duodenum (rabbit) is 0.7° C. higher. These higher temperatures may be due, in part at least, to the proximity of the liver, for, according to Lefevre, the temperature of the liver (of the dog) may be more than 1° C. higher than the rectal temperature.

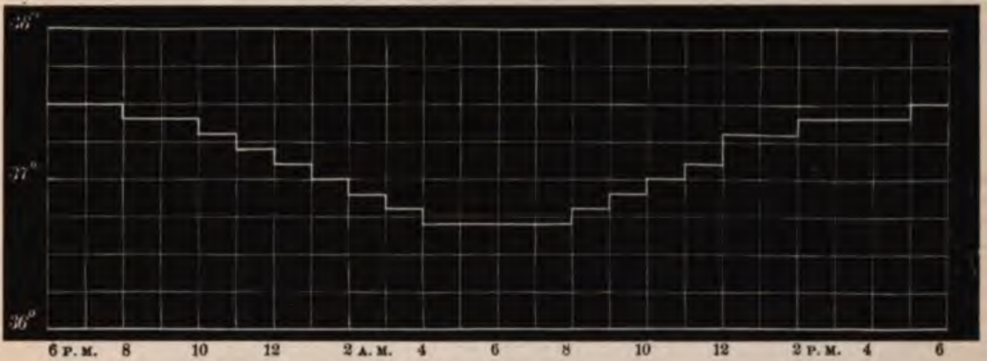


FIG. 147.—The normal diurnal variation of temperature in man, after Jürgensen.

Numerous determinations of the normal body temperature of man have shown that it presents *individual variations* of some tenths of a degree. As a mean value 37.5° C. is given as the temperature in the rectum, 37.2° C. in the mouth, and 37° C. in the axilla. Moreover it is not entirely correct to say that man has a constant temperature. Even if we neglect the variations due to diseases or the diminutions due to excessive cooling of the body, it has been shown that the temperature of man in the course of a day undergoes certain normal variations. The difference between minimum and maximum in a thoroughly healthy individual may amount to 1°–1.5° or more. These variations run a very regular course which, according to Jürgensen, shows a minimum early in the morning from three to six o'clock, increases gradually from that time, and after some fluctuations, reaches a maximum about six to seven o'clock in the evening (Fig. 147).

The *cause of these variations* is primarily the variations in the intensity of metabolism. If the CO_2 elimination, which to a certain extent may be looked upon as an expression of the relative amount of metabolism, be determined at different times of the day, a surprising agreement is found between its course and that of the body temperature (cf. Fig. 148). It should be noticed that the temperature curve in the figure was not taken from the same subject as the CO_2 curve. The discrepancies between the two are no more than can be satisfactorily explained by this circumstance alone.

If the CO_2 output at different hours of the day be obtained on the fasting body in purposely enforced physical rest, it shows, as Magnus-Levy and especially Johansson have pointed out, but very slight variations; and in the course of any given period, the body temperature decreases because of the relatively small metabolism. From which it follows that the above-mentioned variations in the intensity of metabolism are called forth primarily by the variations in the movements and tension of the muscles occurring for one reason or another in the course of the day. A coöperating factor, though not of itself by any means so potent as the muscular work, is the increase of metabolism due to taking food.

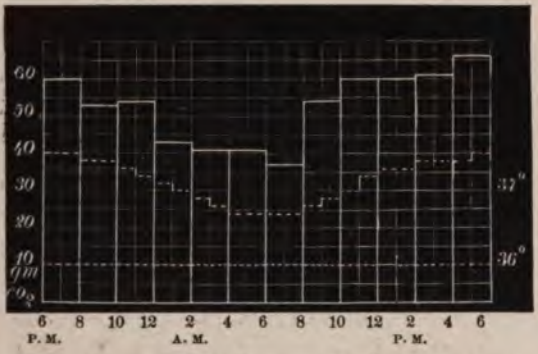


FIG. 148.—The elimination of carbon dioxide in man, determined every two hours. ———— CO_2, in grams. - - - - - - - - - diurnal variation of temperature from the curve by Jürgensen in Fig. 147.

One inference from this view is that with a reversal of the daily habits, the temperature variations ought to be reversed. According to some authors this actually takes place. But Benedict and Snell were unable to observe any perceptible tendency to a reversal of the temperature curve in the case of a man who, for ten successive days, worked at night and slept by day, although the curve did vary decidedly from the normal.

In my opinion one cannot conclude from these observations that other factors than those mentioned above are concerned in production of the daily variations of temperature. In this research the subject slept, as the authors remark, a much shorter time than he was accustomed to, and it is in fact a fairly common experience that a man cannot accustom himself to a reversed mode of life to the extent of completely converting day into night and night into day. On this account the muscular activity cannot be exactly adjusted to the changed order of life. Moreover, we possess observations on monkeys which show that the reversed order does produce a complete reversal of the temperature variations. When these animals were kept for days either in complete darkness or constantly in the light, the normal variations ceased and were replaced by quite irregular ones (Galbraith and Simpson).

Temporary changes of the body temperature in one direction or the other may be produced by various voluntary acts which tend to increase either the heat production or the heat loss. Thus the temperature falls as the result of sitting perfectly still, of drinking cold water, etc.; it rises as the result of muscular work, etc.

However, all these changes in the body temperature are as a rule very insignificant, and this very remarkable fact has been established—that the mean value of the body temperature obtained from a large number of determinations extending over periods of twenty-four to forty-eight hours, remains the same in spite of all such disturbances. This maintenance of the mean body temperature unquestionably is closely related to the fact that, with a free choice of food, and within periods of some days, the body automatically measures out its supply of energy with unerring regularity.

Variations of the temperature between *persons of different age* are but slight. Since the fœtus has a certain small metabolism of its own, its body temperature must be somewhat higher than that of its mother, which direct observations tend to prove. The difference amounts however to only 0.3° C. After birth the temperature of the child sinks from 0.5° to 0.8° C., a fact dependent in part only on the first bath; it returns during the first week, as it appears, with some fluctuations, and then is maintained at the value given above until old age, when the temperature is said to become some tenths of a degree higher.

When the body is subjected to *excessive loss of heat*, it is no longer able to maintain its temperature at a constant level. The lower the temperature of the body falls, the greater are the disturbances thereby produced. The highest nerve centers are the first to suffer from this cooling, but the centers of the medulla which are important for the maintenance of life, are not paralyzed until the reduction has been carried much further. Theoretically it may be assumed that in man restoration is possible from a very considerable reduction of the body temperature, so long as the centers of the medulla have not lost their vitality. Cases have been observed in fact where patients recovered from a fall of the body temperature to 24° C. due to great exposure. Indeed, a case has been reported of a man who retained consciousness with a temperature of only 26.7° C.

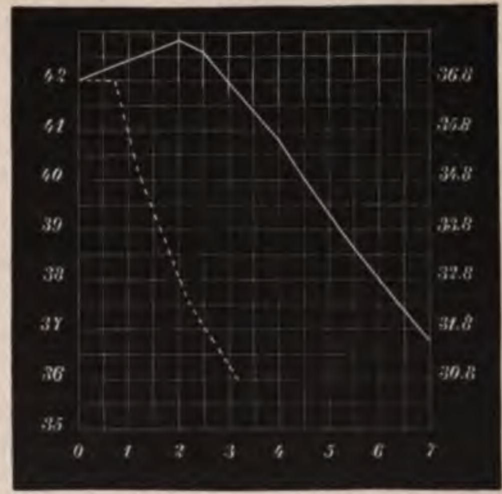


FIG. 149.—The temperature of the body after death (Niederkorn). ————, typhoid fever (the temperature in degrees centigrade is given at the left). - - - - - - - - -, pulmonary consumption (temperature at the right). The abscissæ represent hours after death.

In like manner, an *increase of the temperature*, if it passes a certain limit, which is different for different individuals, involves first disturbances to the general health, and later loss of consciousness, while the centers of the medulla remain functional. In general it may be said that the body stands a fall better than a rise in its temperature. A rise of only 2° or 3° C. causes very severe disorders, and experience has shown that a temperature of 41°–42° C. constitutes a very dangerous symptom. And yet a man can endure still higher temperatures provided they do not last too long. The highest authenticated temperatures of patients who afterwards recovered are: 43.6° C., sunstroke; 44° C., scarlatina, malaria; 46° C., malaria (?).

After death the body of course cools down, but not always immediately. Thus it has been shown that the temperature of a body which has died from infectious fevers or injuries to the brain or medulla rises for a time. This is an indication that the metabolism and consequent heat production do not cease everywhere in the body the moment the patient draws his last breath. Also after death from chronic, long-continued diseases, where no such post-mortal rise of temperature is observed, the manner in which the fall of temperature occurs is evidence that combustion in some organs does not cease the moment of death. We find in such cases that the temperature remains unchanged for a time, or falls very slightly, and then declines rapidly. The first stage can only be explained by supposing that heat production is still going on after death (Fig. 149).

§ 2. THE SOURCE OF ANIMAL HEAT

The *source of animal heat* is the combustion going on in the body (cf. page 46). Inasmuch as combustion takes place in all parts of the body, all the different organs participate in the production of heat. And yet the share of the different organs in this process is very different, since in certain organs metabolism is more active than in others.

The *cross-striated muscles* are the most important in this connection. They constitute about forty per cent of the total weight of the body, and, if we neglect the skeleton, where the absolute quantity of heat produced is not very significant, they constitute fully fifty per cent of the weight.

Even the perfectly quiescent muscles generate heat. Meade-Smith determined simultaneously the temperature of the blood in the aorta and in the leg muscles, diverting the blood meantime from the muscles. He was able to show that the temperature of the muscle at the beginning of five-minute periods without blood was as a rule higher, and at the ends of these periods invariably higher than the temperature of the blood in the aorta; also that the temperature of the muscle always rose during the period. The increase might amount to 0.1° C. and the difference between muscle and blood might at the end of the period be 0.6° C. Then with every muscular contraction, as work is performed, additional heat is generated. Indeed the energy consumed as work is never more than a fractional part of that which appears as heat (cf. page 113).

Next to the muscles, *the glands*, especially the liver, stomach and intestines, are great producers of heat; but no great importance is to be ascribed to the bones (except the red marrow), the skin or the lungs. Very active metabolism takes place in the gray matter of the central nervous system. But since the metabolism in the white matter is very slight (cf. Chapter XV), and since the entire nervous system amounts to only about 1.9 per cent of the body weight, it is not to be supposed that this system produces any considerable fraction of the total quantity of heat formed. It is not yet possible to determine more accurately the share of the different organs in this important function.

§ 3. LOSS OF HEAT FROM THE BODY

The heat formed in the body is partly utilized in *warming the food*, including water ingested and the air inspired, is partly given off by *conduction and radiation* through the skin, and partly disappears in the *evaporation of water* from the air passages and from the skin, and in the liberation of carbon dioxide from the lungs. The following estimate, agreeing essentially with those of Helmholtz and Rosenthal, indicates approximately the proportion of losses in an adult man by these different avenues.

A. WARMING THE FOOD AND AIR

(1) Water drunk at 15° C. and warmed to 37.5°—raised therefore 22.5°	= 33.75 Cal.
(2) 1,500 g. food eaten at 25° C. (mean) and warmed to 37.5°—raised therefore 12.5°; specific heat 0.8	= 15.00 "
(3) 15,000 g. (= 11,500 l.) air respired at 15° C. and warmed to 37.5°—raised therefore 22.5°; specific heat 0.237	= 79.75 "
	128.70 "

B. LOSS OF WATER AND CO_2 IN THE BREATH

(4) It is assumed that the inspired air is half saturated with water vapor at 15° C., and that the expired air is fully saturated at 37.5° C. Approximately 450 g. of water would be given off, therefore, in the form of vapor from the respiratory passages; the latent heat of the water vapor is 0.537 Cal.	= 241.70 "
(5) The absorption of heat in the liberation of CO_2 from the lungs (800 g.); 0.134 Cal. per g.	= 107.20 "
	348.90 "
From above	128.70 "
Total	477.60 "

The sum of heat losses specified under these five headings amounts to 477.60 Cal. Estimating the total heat loss of an adult man at 2,400 Cal., this sum represents only about twenty per cent of the total. The remaining eighty per cent (in round numbers) takes place through the skin.

The direct calorimetric measurements by Atwater give approximately the same result. In a series of experiments lasting forty days the mean heat loss, in the case of a resting man, by conduction and radiation was 1,669 Cal., through the urine and fæces 31 Cal., by evaporation of water 550 Cal.—i. e., in percentages 74.2, 1.4, and 24.4 respectively. In the case of a man at work, the mean for twenty days by conduction and radiation was 2,277 Cal., through urine and fæces 19, by evaporation of water 1,126; or in percentages, 66.5, 0.6, and 32.9 respectively. The proportion of evaporation from the skin and from the lungs was not determined.

The skin gives off heat to the surrounding air, or to other cold substances coming in contact with the body, by conduction, radiation and evaporation. The relative importance of these factors varies greatly under different circumstances. The quantity of water vapor given off from the skin depends to a great extent both upon the temperature and humidity of the surrounding air, and also upon the heat production going on in the body, which in turn varies with the kind and the quantity of food eaten and the amount of work done.

It is therefore impossible to give definite figures for the amount of water given off through the skin; for all of the twenty-four-hour determinations thus far published have reference only to the total output of water vapor, and not to the apportionment between lungs and skin.

Using the above-mentioned figures (table, page 403) for the output of water vapor in respiration, we can form some approximate idea of the amount of water vapor eliminated by the skin. Some examples are adduced here in which the necessary reductions have already been made. A fasting individual gave off through the skin on the fifth day of his fast approximately 350 g. of water; loss of heat 188 Cal. The same individual on a plentiful diet gave off through the skin 710 g. water, loss of heat 381 Cal., twice as much therefore as in the first case. Another subject at rest and on a moderate diet excreted through the skin 480 g. of water (= 258 Cal.); on the same diet at severe work, 1,280 g. water (= 686 Cal.) (cf. also page 397).

According to Zuntz, soldiers on the march in cold weather eliminate about one-fifth of the total output of water through the respiration, in warm weather only about one-sixth. In extreme cases the loss of heat by evaporation may reach the enormous value of ninety-five per cent of the total heat loss.

The loss of heat by radiation and conduction also exhibits great variations, which depend on the temperature of the surrounding air and the heat production going on in the body, as well as upon the clothing. Both radiation and conduction are considerably greater on exposed parts of the skin than on clothed parts. From experiments on covered portions, the total heat loss by radiation has been calculated for a grown man at about 700–800 Cal., while from observations on the naked skin, it is estimated at 1,700–1,800 Cal. Similar differences have been observed with regard to loss of heat by conduction.

§ 4. PROTECTION AGAINST LOSS OF HEAT

Notwithstanding considerable variations in the temperature of the surrounding air, homoiothermous animals maintain an *even balance between heat production and heat loss.* That this is possible with so small a quantity of heat production in the body is due to the fact that provisions are made in warm-blooded animals for restraining the loss of heat through the skin. These provisions are, (1) the subcutaneous adipose tissue, and (2) the natural hairy or feathery covering of the body.

We have already seen that the muscles come first in the order of heat production. The heat formed in them, however, cannot be readily conducted to the superjacent skin because the intervening adipose tissue is a very poor conductor of heat. A piece of skin 2 mm. in thickness will allow 0.00248 cal. (small) to pass through in one minute, when the difference in temperature is 18.2° C. The same piece of skin plus a 2 mm. layer of fat under the same circumstances will allow only 0.00123 cal. to pass. With less difference in temperature on the two sides the protecting influence of the fat is still greater, so that for example with a difference of 9° C. a layer of fat 2 mm. in thickness retains 0.8 of the total quantity of heat which would otherwise be allowed by the skin to pass through (Klug). In considering the properties of fat deposited at different places in the body, Henriques and Hansen have directed attention to the lower melting point of fat which lies nearer to the outer surface of the body. This is doubtless connected with the fall in temperature met with in passing from the interior toward the surface; for the lower the temperature the lower must be the melting point of the fat in order that it may remain in a fluid state.

The *great importance of the subcutaneous fat* is most beautifully seen in the case of the great warm-blooded marine animals of the arctics. They live habitually among the ice blocks in a medium which conducts heat at least twenty times better than air, and yet they are able to maintain a body temperature of 35°–40° C. The skin is subjected to conditions which would abstract an enormous amount of heat, but the extraordinarily thick layer of subcutaneous fat isolates the muscles and the organs—in short, the real body—from the skin.

For warm-blooded animals which live in the air, the loss of heat is greatly reduced by the hair and feathers; and clothing serves the same purpose for our own bodies.

Air is itself a very poor conductor of heat, but when in motion it may carry away great quantities of heat. Let us imagine a naked man in an atmosphere colder than his skin. The layer of air immediately adjacent to his skin is first warmed by his body and as a consequence it becomes lighter. It rises and is replaced by fresh, cold air, which in its turn is warmed, replaced, and so on incessantly. The body produces therefore by virtue of its own heat an uninterrupted current of air, which abstracts great quantities of heat from it.

This active exchange of air is considerably restricted by the clothing, whatever the material of which it is made, inasmuch as it prevents free access of the air to the skin. The air inclosed by the clothing is relatively stationary and thus, because of its poor conducting qualities, it constitutes a thermally insulating layer around the body. Moreover, not only the air between the clothing and the skin, as well as between the different garments, but the air in the meshes of the clothing material itself is to be taken into consideration. For clothing materials, like hair and feathers, are of themselves much better conductors than air. The amount of air held in the meshes of the clothing of a man as ordinarily dressed (excluding wraps) is estimated at 20–30 l. (Rubner).

Important as this layer of surrounding air is, it must not stand absolutely still, but must be kept in continual motion, even if it be very slow motion; for otherwise the air very quickly becomes saturated with water vapor given off by the skin, and then no further loss of water vapor can take place. The result is great discomfort and, under some circumstances, great disturbances in the regulation of heat.

The loss of heat by radiation is likewise reduced considerably by the clothing. Since the clothing materials consist of substances which do not permit the passage of radiant heat, they absorb the heat radiating from the skin and are themselves warmed by it. Consequently this heat remains longer in the neighborhood of the body and thus helps to warm the air immediately surrounding it. When one feels that he is losing heat from the immediate neighborhood of the body too rapidly, he covers the garment from which the heat is escaping with still another, which catches the heat radiating from the first and delays it still longer. A shirt, vest, coat, etc., act in this way.

The radiation of heat from the skin is still further diminished by water vapor, because it reduces the diathermic capacity of the air.

As a result of these protective measures, the temperature of the air immediately surrounding the body is generally somewhat above 30° C. The skin itself in places where it is clothed has a temperature of 33°–35° C., on naked places its temperature is lower (cf. page 399).

That warm-blooded animals can maintain a constant body temperature, when exposed to a very low external temperature, is due to their natural or artificial clothing. This is perfectly evident from the fact that the temperature of an animal declines more or less when it is shorn, as well as by the experience that a naked man at rest can only maintain his temperature at the normal level when the surrounding temperature is at 27° C. or higher (Senator).

By experiments with the calorimeter Rubner has determined the saving of heat to the body accomplished by clothing in some special cases. A guinea pig lost normally by radiation and conduction on the average 3.37 Cal. per hour; after being shorn the hourly loss was 4.19 Cal.—i. e., 33.3 per cent more. In the human subject the loss from the naked arm by radiation and conduction at ordinary room temperature was about thirty per cent more than that from the clothed arm.

And yet the saving actually accomplished by the clothes is somewhat less than this would indicate; for the output of water vapor from the clothed body is greater than from the naked because of the higher temperature of the air immediately adjacent to the skin. From experiments on the naked forearm and on the hand it has been found that in a dry atmosphere at a temperature of 15°–20° C. about twenty per cent of the total heat loss takes place by evaporation. From the naked arm the elimination of water amounted to 3.59 g., and from the clothed arm 4.39 g.—a difference of twenty-two per cent. Using this value the saving of heat due to clothes may be calculated as follows:

The total loss of heat through the skin	100
By radiation and conduction	80
By evaporation	20
The loss by radiation and conduction is diminished by the clothes twenty per cent, leaving therefore	56
While the loss by evaporation is increased twenty-two per cent making	24
Total	80

The saving according to this amounts to about twenty per cent at ordinary room temperature, and of course at lower temperature is much greater.

Just as man seeks to reduce as much as possible the loss of heat during the winter by wearing heavier clothing, so the animals offset the influence of the lower temperature by a thicker coat of hair or feathers. What this thick coat actually does for its owner may be seen in polar animals living in the air, which maintain a normal body temperature even at an external temperature of −40° C. (Parry).

§ 5. REGULATION OF THE BODY'S TEMPERATURE

The facts thus far discussed relate only to the necessary conditions for the maintenance of the body temperature, but by no means suffice to explain this phenomenon theoretically. For, while both animals and men are all the time being exposed to greater or less variations in the temperature of the surrounding medium, neither the thickness of the clothing nor that of the adipose tissue is being changed to correspond with these variations; and yet the body maintains its temperature unchanged. The sum total of all those processes by which this constancy is maintained is comprehended under the term *heat regulation* of the body. These processes can be divided into two groups according as they relate to heat production or to heat loss.

The way in which the production of heat varies under the influence of the surrounding temperature has been already presented in Chapter IV (page 114). But heat production is influenced also by the *amount of food*, and in controlling the latter we have a means of adapting the transformation of substance in the body to the requirements of heat regulation.

A noteworthy illustration is given by K. E. Ranke, who studied his diet both in Germany and during a scientific expedition to Brazil. Allowing himself free choice of food, the amount being controlled only by his appetite, his total intake between the temperatures of 15° and 22° C. was on the average 3,300–3,500 Cal. In a dry climate at a temperature of 25° C., it fell to 2,800 Cal., and at an atmospheric temperature of 25°–28° with a humidity of about eighty-three per cent, it reached the low level of 1,970 Cal. (= 26.9 Cal. per kg. body weight). His body weight decreased however on this low ration. In order to recover his original weight he was obliged to adopt a richer diet, but various disturbances in his general health appeared while he was experimenting in this direction.

A. REGULATION OF HEAT LOSS

As we have seen above the temperature of the skin depends primarily upon the blood supply; the greater the amount of blood flowing through it, the warmer it becomes. But the warmer the skin becomes, other conditions being the same, the greater is the loss of heat from the skin by radiation and conduction. The heat loss by radiation and conduction therefore depends upon the *amount of blood supplied to the skin.*

The blood vessels of the skin, like the other vessels of the body, are under the *influence of the vasomotor mechanisms*, and are constricted or dilated according to the momentary requirements of the heat regulation. Thus in cold weather and when the production of heat in the body is not greatly increased by muscular work, they are constricted; and in hot weather they are dilated.

These changes in the blood supply of the skin serve in another, and perhaps still more important manner, to regulate the loss of heat. During its flow through the cutaneous vessels, the blood naturally gives off heat, and returns to the interior somewhat cooled. When the vessels are dilated, more blood flows through them, and more heat is thus lost than when they are constricted and the quantity of blood flowing through them is small. While the cutaneous vessels are constricted, the vessels of the abdominal viscera and, as it appears from the investigations of Wertheimer, those also of the muscles —i. e., of the most important heat-producing organs—are dilated; while during dilatation of the cutaneous vessels, those of the abdominal viscera are constricted.

Experience proves that a man can maintain his body temperature without increase in an atmosphere whose temperature is *much higher than that of his body.* This appears the more remarkable when we consider that the metabolism and heat production of the body never cease, however high the surrounding temperature may be. The fact, as was first observed by Benjamin Franklin, is to be explained by the secretion of sweat. At a higher atmospheric temperature the sweat glands are stimulated, and evaporation of the sweat thus poured out upon the skin absorbs a large quantity of heat from the body. In this way the body is cooled and maintains its temperature unchanged, whether the outside temperature exceeds or only approaches that of the body.

But the amount of sweat secreted depends not only upon the temperature of the air, but also upon the *amount of heat being produced* in the body at the time. If the heat production of the body be considerably increased as the result of severe muscular work, the body will sweat even at an atmospheric temperature of 0° C. After a full meal, owing to the increased heat production a greater quantity of sweat is secreted than when the metabolism is reduced for lack of food.

B. CENTERS FOR HEAT REGULATION

Among the many so-called "heat centers," located in different parts of the central nervous system, which have been mentioned by different authors, only a single one seems to be fairly entitled to the name. If a fine needle be thrust into the brain from above downward in such a direction as to strike the medial edge of the *corpus striatum,* a rise in temperature appears in the skin, in the muscles and in the rectum; likewise an increase of metabolism and of heat loss as determined by the calorimeter (Aronsohn and Sachs, Richet). The increase of temperature amounts to more than 2° C., the increase of metabolism and of heat loss to about 20 per cent. The maximum effect appears within twenty-four to seventy-three hours after the puncture, unless the needle be pressed through to the base of the cranium, in which case it appears within two to seven hours. The results of electrical stimulation by means of electrodes insulated to the ends show that the effect of puncture is due to stimulation and not to destruction of the parts encountered.

We cannot form any definite opinion at present, as to the significance which this and other "heat centers" have in the regulation of this important function.

How the centers for heat regulation (wherever they may be located) are stimulated, is another question which cannot be conclusively answered as yet. It is indeed fairly certain that the cold and heat nerves of the skin play a great part, since heat production and heat loss are reflexly influenced in one direction or the other according to conditions reported by these nerves. Changes in the temperature of the blood also might play a part; that is, cold might by direct action on the heat centers bring about an increase of metabolism and a constriction of the cutaneous vessels, or warmed blood might rouse the sweat centers to increased activity. This mechanism does actually participate in some such way in the regulation of heat, for in muscular work the sweat breaks out only when the body temperature has increased 0.3°–0.5° C. (Fredericq). Likewise the augmented respiration appearing with a high external temperature (page 318) is caused by a direct exciting effect of the blood, for it can be reproduced in all its essential features by locally warming the blood in the carotids on the way to the brain; but it will not appear, notwithstanding a very strong heat stimulus, when the head is cooled.

The ability to maintain a constant temperature in certain species of animals, including man, is not fully developed immediately after birth. In such warm-blooded animals as have a well-developed nervous system at birth—e. g., guinea pig and chick—the heat-regulating mechanism also is completely functional at this time. But those which, like rats and pigeons, are born blind and helpless, only acquire the power of regulating their own temperature in the course of the second week (Pembrey). The newborn child also has not yet come into full possession of its power to regulate its heat (Raudnitz). It is probable that this post-embryonic development of the regulatory mechanism is intimately connected with the development of the neuromuscular apparatus going on at the same time.

CHAPTER XV

THE FUNCTIONS OF CROSS-STRIATED MUSCLES

THE purpose of the cross-striated muscles is twofold: first to provide for the bodily movements, and secondly to participate in the production and regulation of heat in the body. In this chapter we shall first inquire into the general properties of the muscles and shall then briefly discuss their relations to other organs.

FIRST SECTION

GENERAL PHYSIOLOGY OF MUSCLE AND NERVE

Inasmuch as the general properties of muscles and of nerve fibers agree in many respects, and the information gained from nerves very often throws light on the corresponding phenomena of muscles, it seems best to discuss them here together.

Physiologists have for a long time given preference to the study of the general properties of muscles and nerves because at first it promised to yield very important results bearing on the fundamental properties of the living substance in general. A great number of facts have been collected by the work done in this field, but unfortunately they do not as yet afford us a basis for any consistent theory of nervous and muscular activity. Significant as these facts are, we must be content to mention only the most important of them, a more exhaustive presentation being quite beyond the possibilities of a text-book of this size.

When not otherwise expressly stated, the facts given may be understood as applying to the surviving nerves or muscles of the frog, exsected from the body (cf. page 6). A motor nerve is generally employed in investigation of the general properties of nerves, and in most cases the muscle connected with it serves as the indicator of the state of the nerve. The changes in the form of the muscle are usually registered by the graphic method (cf. page 6).

§ 1. FUNDAMENTAL LAWS OF NERVOUS ACTIVITY[1]

A nerve is *irritable* to ordinary artificial stimuli at all points of its course, and it transmits the stimulus in both directions from the point of stimulation. This is best shown by means of the action current (page 48). If a nerve be stimulated at its middle, each of the two ends being at the same time connected with a galvanometer, the action current appears in both. This is true not only of mixed nerve trunks composed of both afferent and efferent fibers, but can be demonstrated on the anterior roots of the spinal nerves which contain only efferent fibers (Du Bois-Reymond).

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[1] The properties of different kinds of nerve fibers will be discussed more fully in Chapter XXII.

If a living nerve be severed, it of course no longer has the power to transmit the stimulus. But the same is true if the nerve be simply tied off. To be capable of conducting, a nerve *must, therefore, be intact,* not only in the physical, but also in the physiological sense.

The *conductivity* of a nerve may be diminished or abolished for a time by various agents: external pressure—e. g., when, as we say, the limbs "go to sleep"; chloroform; alcohol, etc. All such agents have this in common, that they reduce or even abolish the physiological continuity of the nerve, without destroying its physical integrity. And yet the local excitability of the nerve in the same place may persist. Under certain circumstances it may happen also that a segment of the nerve, which for some reason is not excitable, still has the power to transmit the stimulus received at some other point on the nerve. This is witnessed, for example, in certain stages of regeneration of a nerve that has been cut. Moreover, the *excitability* of the nerve does not always keep even pace with its *conductivity,* possibly because the nerve responds in a different manner to its natural stimulus propagated from one segment to another, from what it does to the artificial stimuli.

A stimulus once received by a nerve fiber is transmitted only within the same fiber and its branches, never passing to the fibers running beside it in the same trunk (law of *isolated conduction*).

This law holds also for the conducting pathways in the central nervous system. One can convince himself of its validity in a very simple way. If, for example, he touch the tip of his tongue, at each of two places about 1 mm. apart, with a sharp point, he can distinguish the two points very accurately, which of course would not be possible if the two stimulated the same nerve fiber.

In very close relation with this law belongs the discovery of the *specific character of the response* to excitation—i. e., that stimulation of a definite nerve produces an effect in its own answering organ and in that organ only. By the *answering organ* we mean that particular organ connected with the nerve and specially influenced by it. The answering organ of an ordinary motor nerve is the muscle which it innervates, the answering organ of a secretory nerve is the gland which it controls, etc. The answering organs of the afferent nerves are nerve cells situated in the central nervous system. From these new nerve paths originate, and end in other nerve cells, and thus stimulation of a single afferent nerve may rouse a whole series of different nerve cells united together. Finally, a nerve cell connected with an efferent nerve may be set in action by an afferent nerve, and a peripheral organ may thus be stimulated without the participation of the will or even of consciousness. Such a phenomenon we call a *reflex* (Chapter XXII). Because of the manifold way in which the nerve fibers are combined with one another in the central nervous system, very complex effects may result from a single afferent stimulus, without in any way invalidating the law of specific response.

§ 2. THE PROPERTIES OF RESTING MUSCLE

A. ELASTICITY

If a metallic wire vertically suspended be loaded with a certain weight, almost immediately it assumes the maximum length for that load and, practically speaking, is not extended further however long the weight remains. A muscle or other organic tissue behaves very differently. If we load a fresh muscle with a weight, for a moment it takes a certain length according to the size of the load, but thereafter as long as the weight remains it continues to stretch, at first rapidly and then more and more slowly. This secondary stretching is spoken of as the *after extension.* When a muscle already stretched by a certain weight is unloaded, it shortens rapidly at first, then more and more slowly. In this case it is said to exhibit secondary elasticity, or *after shortening* (Fig. 150).

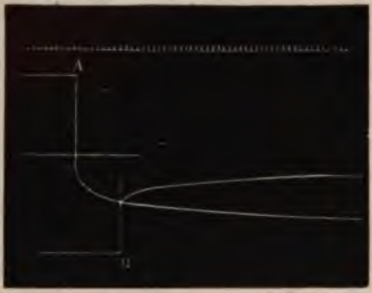

FIG. 150.—Curves representing the extension, *A*, and elastic shortening, *B*, of two adductor muscles, after Blix. *A* was suddenly loaded with 100 g. of weight and *B* was suddenly relieved of its weight.

These secondary phenomena render the investigation of the elasticity in muscles and the influence of load rather difficult. In order to reduce the effect of after extension as much as possible, Marey and Blix have hit upon a device by which the load can be increased or diminished continuously and very rapidly, and the variations in length of the muscle can be recorded at the same time (Fig. 151).

The support (*i*) bears the muscle lever (*c*) on which the muscle is fastened at *m*. The lever is loaded by means of the weight *h*, and is counterbalanced by the weight *k*. The plate (*f*) with the recording surface (*l*) attached to it can be moved back and forth between the two ledges screwed fast to the base. At the same time the weight *h* controlled by the bar *b* is moved along the lever, and in this way the load acting on the muscle is changed in proportion to the excursion of the writing surface. Curves obtained with the apparatus represent the extensibility and elasticity of the muscle with a uniformly increasing and uniformly diminishing load.

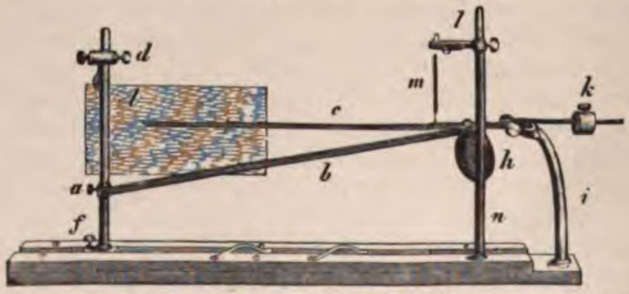

FIG. 151.—Apparatus of Blix and Lovén for recording the elasticity curve of a muscle.

Such a curve is given in Fig. 152. We see that the increase in length of the muscle with a load increasing at a uniform rate is less, the greater the absolute load—i. e., the coefficient of elasticity becomes greater as the tension of the muscle increases. Moreover, it appears from the figure that the elasticity curve runs below the extension curve, a circumstance not due to after extension. The elasticity, it will be observed, is very complete, since the muscle when it is released resumes its original length. Permanent lengthening appears to a noticeable extent only when the muscle substance is torn by too great an extension.

B. CHEMISTRY OF MUSCLE

The reaction of fresh, resting muscle was for a long time regarded as acid. But Du Bois-Reymond pointed out that the reaction of the flesh of different mammals is more or less alkaline. Further investigation has shown that there is no one reaction for resting muscle, but rather two: alkaline to lacmoid and neutral or faintly alkaline to curcuma. The aqueous extract of cross-striated muscle reacts in the same way. According to Röhmann, the acid reaction of the water extract to curcuma is essentially due to sodium monophosphate, and the alkaline reaction to lacmoid to the acid carbonate of sodium, to the diphosphate of sodium and to alkaline compounds of the proteids.

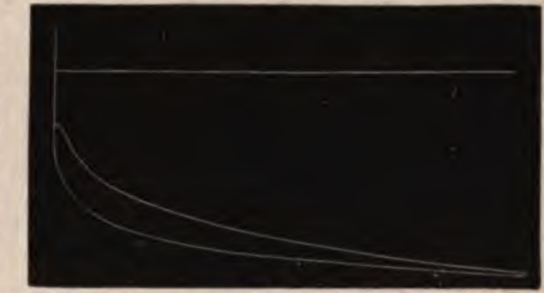

Fig. 152.—Extension and elasticity curves of the frog's gastrocnemius, after Nerander. This tracing was obtained with the apparatus shown in Fig. 151. The upper line represents the curve of extension and the lower line the curve of elastic shortening.

Among the proteids which make up the insoluble *stroma* of muscle, there are two bodies, one a globulin (*myosin*, v. Fürth; *paramyosinogen*, G. N. Stewart) and the other a globulin-like substance (*myogen*, v. Fürth; *myosinogen*) which can be extracted from fresh, blood-free rabbit's muscle with normal salt solution. In dead muscle both pass over spontaneously into insoluble modifications (myosin fibrin and myogen fibrin) but they are distinguished by their precipitation reactions and the temperature at which they coagulate. Myosin coagulates at 44°–50° C., myogen at 55°–65° C. Of the total quantity of proteid which goes into solution with normal salt, myosin constitutes about twenty per cent and myogen about eighty per cent (v. Fürth).

Other nitrogenous constituents of muscle represent the decomposition products of proteid: creatin (0.1–0.4 per cent in fresh muscle), hypoxanthin, xanthin, and guanin (0.23, 0.05 and 0.02 per cent of dry substance respectively). Here belong also the phosphocarnic acid (0.1–0.2 per cent); inosinic acid ($C_{10}H_{13}N_4PO_8$) from which hypoxanthin can be split off; carnosin ($C_9H_{14}N_4O_3$) closely related to arginin; and carnin ($C_7H_8N_4O_3$).

The nonnitrogenous organic constituents are: inosit (hexa-hydroxy-benzol, $C_6H_6(OH_6+H_2O)$, glycogen, sugar, fat, etc.

Muscles owe their color to a peculiar red pigment (myochrome) which is closely related to hæmoglobin but does not agree with it spectroscopically (K. A. H. Mörner).

§ 3. STIMULATION OF MUSCLES AND OF NERVES

A. THE MUSCLE CURVE

1. *Method.*—A muscular contraction can be recorded in several ways which differ in principle but which finally reduce to two groups, according as the shortening induced by the stimulus is allowed to take place or not. In the latter case the tension of the muscle increases as a result of the excitation, but its length remains constant. For this reason such contractions are called *isometric* contractions, and the variations of tension are recorded after Fick's method as follows (Fig. 153). The muscle (M) is attached to a strong steel spring (*f*) which bears a long writing point (*h*) for magnifying and recording its movements. When the muscle is stimulated, it attempts to bend the spring, but since the latter yields but slightly, the muscle cannot shorten to any appreciable extent; consequently the whole effect of the muscular activity is to increase the tension.

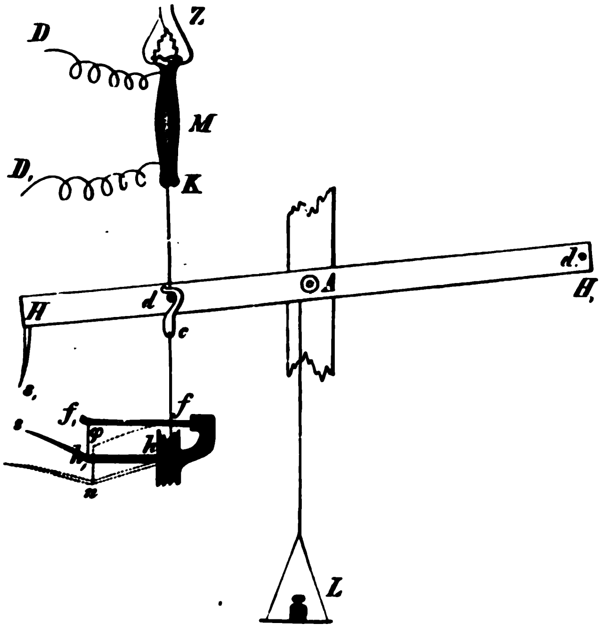

Fig. 153.—Apparatus of Fick for recording variations in the length and in the tension of a muscle artificially stimulated. By unhooking the tension recorder the lever, *HH*, is allowed to move freely up and down like an ordinary muscle lever. For further explanation, see text.

In the other method a lever loaded with a weight is commonly used, and the weight is so chosen that the effort of the muscle to shorten when stimulated is effective. The lever is lifted, therefore, and the resulting curve is a record of variations in the length of the muscle during the contraction.

A loaded lever lifted in this way suffers a certain acceleration in its movement upward, which is often so great that from a certain moment onward the lever moves of its own inertia, and not at the instance of the muscle. It is evident that a muscle curve recorded under such circumstances can be trusted only for information as to the very beginning of the contraction. In order to prevent this "throw" due to inertia a very light lever is employed, and the load is applied as near to the axis as possible (Fig. 160), while the muscle is attached at a greater distance therefrom. Since it is assumed that the tension of the muscle remains the same throughout, this sort of a contraction is called *isotonic*. An actual condition of isotony, however, is scarcely ever to be had (cf. page 435).

To be able to analyze the temporal course of the muscular contraction exactly, one must record it on a writing surface moving with sufficient speed (300–600 mm. per second).

2. *The simple contraction.* The muscular contractions caused by the various stimuli are either *simple* or *summated*. By simple contraction, or merely contraction, we mean that act of the muscle which is discharged by a single stimulus. By summated contractions we understand the contractions discharged by a series of stimuli following each other in rapid succession (cf. page 51).

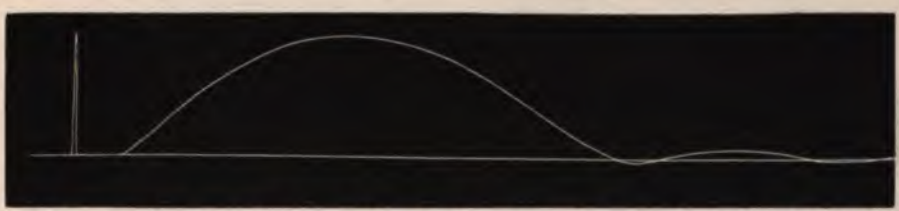

FIG. 154.—Simple contraction curve of the frog's gastrocnemius. The vertical line at the left marks the movement of stimulation. The interval between this line and the point at which the contraction curve leaves the base line is the latent period.

When a muscle receives a stimulus, a measurable time always elapses between the instant of stimulation and the appearance of a visible effect, and this time is designated as the *latent period* (Helmholtz, 1850).

The general procedure in making exact determinations of this as well as of other physiological periods may be explained by the following method: On the lower edge of the drum of a kymograph a metallic peg is securely fastened, so that when the drum is revolving this peg can break an electric contact. The contact forms a part of the primary current to an induction coil. If now the secondary current be conveyed to the muscle, and the drum be set going so that the muscle lever makes a tracing, it is clear that the instant the peg opens (or closes) the primary current the muscle will receive a shock. But it is equally clear that, owing to the latent period, the instant the resulting contraction begins will not be the instant of stimulation. To find on the tracing the instant when the muscle receives the shock, let the drum be moved very slowly until the peg once more breaks the primary current. Since the drum is now as good as standing still the resulting contraction will trace a vertical line (Fig. 154) which marks the instant of stimulation. The interval between this vertical line and the rise of the muscle curve above the base line is the latent period. The period can of course be measured in fractions of a second if the vibrations of a tuning fork be recorded while the drum is going at the same rate of speed. Sometimes it is difficult to say just when the muscle curve rises from the base line. The exact moment can be determined if the experiment be so devised that the muscular contraction, the instant it begins, opens the current to an electric signal.

The *length of the latent period*, which has generally been determined on the frog's muscle, depends upon various circumstances. With a maximal break induction shock and at ordinary room temperature (17°–19° C.), the mean length is about 0.004 second; at a higher temperature it is shorter, at a lower temperature longer. The latent period increases also as the height of the contraction decreases. On the other hand, under circumstances otherwise the same, it is influenced very little by the load or by the tension of the muscle (i. e., up to a certain limit).

If a muscle prepared for stimulation be placed in a horizontal position and a lever be attached to each of its two ends in such a way that any increase in the thickness of the muscle at either end will be recorded, and if the muscle be now stimulated at one end, it is found that the response spreads from the point of stimulation throughout the muscle at a measurable rate of speed (Abey). This *rate of propagation*, which according to Engelmann is independent of the strength of the stimulus, amounts in the frog muscle to 3–4 m. per second (Bernstein, Hermann), or 5–6 m. (Engelmann), and in human muscles to 10–13 m. per second (Hermann).

If in an experiment like the one cited above for the determination of the latent period, the two electrodes be placed on opposite ends of the muscle, the excitation will start from the negative electrode (cf. page 59), and will spread from there throughout the muscle. But before the lever can be raised, the excitation must have reached the entire muscle; whence it is evident that the *mechanical latent period* of the part first excited must be shorter than that indicated for the whole muscle.

After the latent period the muscle curve rises to its maximum height and then falls. Accordingly in every muscular contraction we have to distinguish: (1) latent period, (2) period of shortening, (3) the summit, and (4) the period of relaxation. In the frog's gastrocnemius the period of shortening lasts 0.05–0.07 second, the period of relaxation somewhat longer.

The course of the simple contraction may be very different in different muscles, and in point of time we meet with all possible gradations from the extremely short twitch of certain insects' muscles, lasting only 0.0033 second, to the contraction of smooth muscles continuing for several seconds.

Ranvier first directed attention to the fact that the skeletal muscles of the same animal which differ in color, differ also in their physiological properties. Thus in such animals as the rabbit, we can easily distinguish *red* and *white* muscles. With the red the latent period is longer, the height of the contraction is less—the descending limb of the curve especially being very much drawn out; but the force and endurance are greater than in the white muscles. The former are therefore more capable of severe work. Grützner showed later that individual muscles generally are composed of red and white sections, and that the mixture of the two kinds of fibers is often very intimate.

B. RATE OF TRANSMISSION OF A NERVE IMPULSE

It is necessary for the sake of a more complete study of the excitation of nerves that we discuss here the rate of transmission of the stimulus within them. The first researches bearing on this subject we owe again to Helmholtz. The principle of his method is very simple. The latent period is determined as above described, but instead of stimulating the muscle directly the stimulus is applied to its nerve: (1) as near as possible to the muscle and (2) as far as possible from it. We find that the latent period is greater in the second case than in the first. If the two contractions are the same size (Fig. 155), this difference can only be due to the greater length of nerve traversed by the stimulus in the second case. Knowing the difference of length in millimeters and the difference of time in hundredths of a second, we can easily calculate the rate of transmission in meters per second. In the motor nerves of the frog at room temperature this rate is 20–26 m. per second. At lower temperatures it is less; besides, there is a certain dependence upon the strength of the stimulus, a stronger stimulus increasing the rate sometimes very considerably.

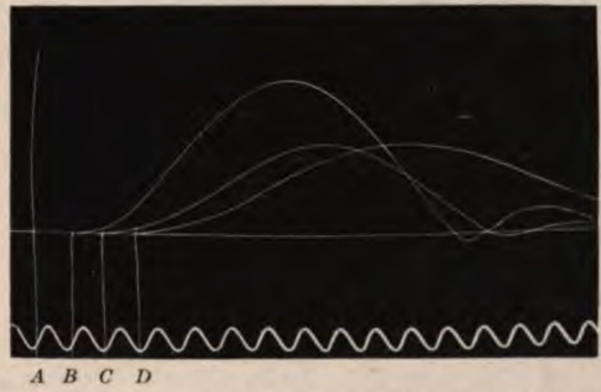

FIG. 155.—Curves illustrating the method of determining the rate of conductivity in the sciatic nerve of a frog. *A*, marks the point of stimulation. The first curve which leaves the base line at *B* (really a little farther to the right than indicated) was obtained by direct stimulation; the second curve (*C*) was obtained by stimulating the nerve as close as possible to the muscle; the third curve (*D*) by stimulating the nerve as far away from the muscle as possible. The lag of the third curve behind the second should give the time necessary for the stimulus to travel from the second point of stimulation on the nerve to the first point—in this case about 55 mm. Since one complete vibration of the tuning fork (below) represents $\frac{1}{200}$th of a second and this is (almost exactly) the time from *C* to *D*, the rate of transmission in this particular case is only about 11 meters per second (200 x .055).

In the invertebrates the rate is very much lower and appears to be less the slower the normal movements of the animal. In a mussel (Anodonta) it is only 1 cm. per second, in an octopus 3–5 m. per second. The nonmedullated fibers of the olfactory nerve of a fish (pike) transmit a stimulus at 20° C. at the rate of 14–24 m. per second (Nicolai).

By recording the contractions of the muscles in the ball of the thumb on stimulation of the median nerve at different points the rate of transmission in *human motor nerves* has been estimated at 33 m. per second. Lately much higher figures, up to 66 m. per second, have been given.

The stimulus passes from the motor nerve to its muscles through the motor end plates. Here a delay is experienced which with a maximal stimulus amounts to about 0.002–0.003 of a second (Bernstein).

C. MECHANICAL STIMULATION OF NERVES

All kinds of mechanical disturbances, provided they take place with sufficient abruptness, have a stimulating effect on a nerve.

A light hammer let fall from different heights upon the nerve, resting upon a solid support, is commonly used for demonstrating the mechanical stimulation. If the nerve be subjected to a slowly increasing pressure or tension, its excitability at first increases, then as the pressure or tension becomes still greater it falls. Beyond a certain limit pressure applied to a nerve entirely abolishes its power of conducting impulses (see page 411). According to Kühne and Üxkull, stimulation may occur on releasing a nerve from pressure.

D. ELECTRICAL STIMULATION OF MUSCLE AND NERVE

1. *Method.*—The kinds of electrical stimuli the effects of which have been most fully studied are the constant and induction currents.

In applying the electric current to a muscle or nerve, or in leading off electrical currents generated by animal tissues to a galvanometer, ***nonpolarizable electrodes*** are used wherever it is practicable. Metal electrodes—e. g., of platinum—are not well adapted to such a purpose, partly because it is difficult to find two pieces of metal between which there would be no differences of potential, and partly because the contact of such electrodes with moist animal tissues may very easily set up a difference of potential. In either case the nerve would be subjected to an extraneous current generated by the electrodes themselves, which often perhaps would make no essential difference in the results of the experiment, since such a current would necessarily be very weak; but in many investigations, especially when exact determinations of potential differences aris-

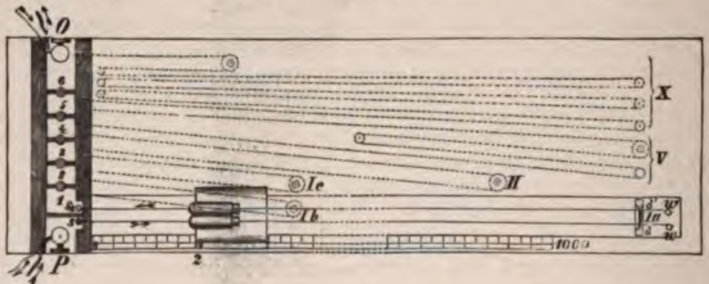

FIG. 156.—Schema of the rheocord of Du Bois-Reymond. The battery wires and the electrodes are connected with the rheocord by means of the binding posts *O* and *P*. The current coming to the binding post *P* splits into two lesser currents, one going through the rheocord, the other through the electrode. The strength of current which will pass through the electrodes will depend on the amount of resistance in the rheocord. This resistance is increased by moving the slide 2, from left to right, also by throwing into the circuit other coils of wire by means of the metal connections 1, 2, 3, 4, etc.

ing in the nerve, muscle, etc., are desired, the polarization, which after a time would be produced by the extraneous current, would greatly vitiate results.

The discovery by Jules Regnauld that zinc in a concentrated solution of zinc sulphate gives no polarization was of very great service in the development of the methods of general nerve-muscle physiology. The fluid, however, must not come in contact with the animal tissues, for they are completely destroyed by so concentrated a solution. The current therefore is applied to the tissues through porous-clay points molded into a suitable shape, and soaked with 0.6-per-cent solution sodium chloride (Fig. 157). Such a mass is but slightly polarizable. Often the clay tip is sealed into the end of a glass tube filled with zinc-sulphate solution into which amalgamated zinc bars connected with the source of electricity are dipped. The boot-shaped electrodes represented in Fig. 157 themselves serve at once as the clay tip and the containers for the zinc sulphate. When it is desired to localize the stimulus, or the connection with the galvanometers very sharply, the tissue is connected with the porous-clay tips of the nonpolarizable electrodes by means of woolen threads wet with 0.6 per cent NaCl.

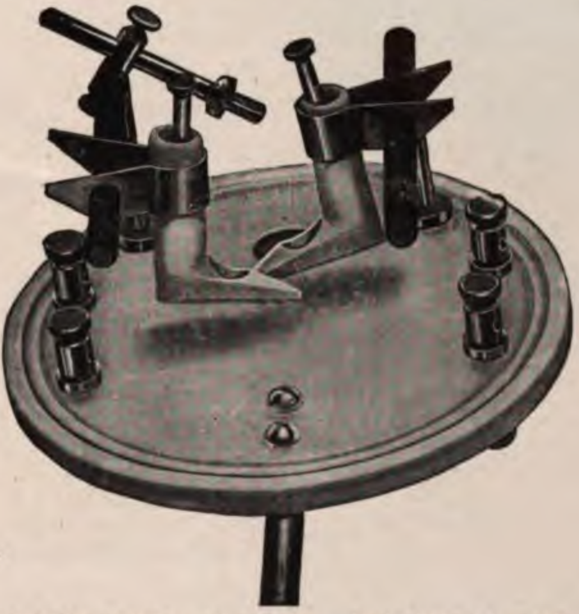

FIG. 157.—Nonpolarizable electrodes, after Porter. Each electrode consists of a porous clay "boot," which may be filled with saturated solution of Zn SO_4. Connection with the battery is made to the zinc bars placed inside the boot. A hollow place on the surface of the "toe" is filled with normal saline and the nerve is laid across those two reservoirs in such a way as to keep it continually moistened with the saline. The entire nerve-muscle preparation can be kept moist by covering boots and all with a glass top which fits in the groove around the edge of the porcelain base.

It is presumed that the student is already acquainted with the principles of the *induction coil.* If not, a text-book of physics should be consulted.

Since the strength of the induction current depends on the abruptness with which the primary current is changed, it is very important that closing and opening the circuit should take place with equal precision. Many different kinds of keys have been devised to supply this requirement; one is shown in Fig. 160.

Often it is necessary to have the stimuli follow one another very rapidly. The device most commonly employed for this purpose is that known as the Wagner hammer (Fig. 159). The current, starting from the battery *K*, passes through the post *g*, the spring *h* provided with an armature, and the screw *f* to the primary coil *c*, and from there through the electro-magnet *b* back to the battery. If the current is closed at the screw *f*, *b* is magnetized and draws the armature of the spring *h* down; in this way the current is broken at *f*, the magnet consequently is demagnetized, the spring *h* is released until it again touches *f*, when the current is once more closed, and so on. The number of interruptions per second can be varied by the position of the screw *f*. The make and break shocks from such an interrupter are not, however, of equal strength. In order to equalize them a side wire is inserted between *g* and *f* and the screw at *f* is raised until the hammer can no longer touch it. The screw *f′* on the other hand, is raised so that the spring in its downward motion comes in contact with it. Now when the hammer vibrates the primary current is never entirely broken, but varies between two extreme values. Consequently the make and break shocks are weaker but (for reasons which we cannot go into here) they are also more nearly equal in strength.

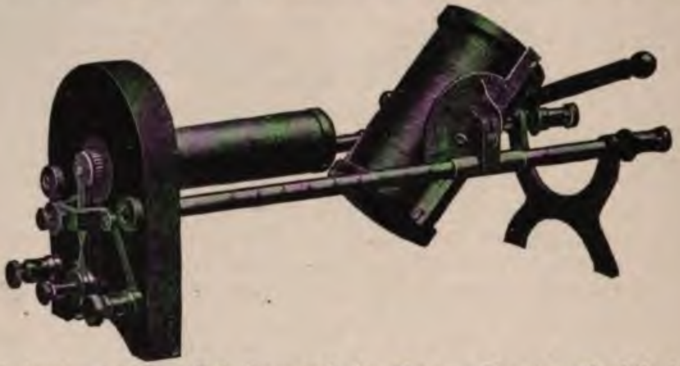

FIG. 158.—Induction coil of Du Bois-Reymond, after Porter. The strength of the induced currents is varied by sliding the secondary coil on the horizontal bars and also by revolving it about its axis.

2. *The General Law of Electrical Stimulation.*—All the effects of an electric current upon the medium through which it flows depend upon the strength and the density of the current. With the same conductor the density of course is directly proportional to the strength.

In 1843 Du Bois-Reymond, on the basis of his discoveries concerning the electrical stimulation of motor nerves, laid down the following general law: The electric current does not stimulate by means of its absolute density, but by means of the alterations which it undergoes from one moment to another; hence the impetus toward a movement which results from these alterations is greater the more rapidly they occur, or the more extensive the alteration in a unit of time. The contraction of a muscle produced by an increasing density of the current was called the "*closing contraction,*" that produced by decreasing density, the "*opening contraction.*"

This law was supported by such facts as the following: a current passing through a nerve may, if increased very gradually, reach a high density without producing any contraction; whereas a much weaker current closed suddenly produces a maximal effect. And conversely, a stronger current if reduced very gradually, may be brought down to *nil* without causing an excitation; whereas the sudden opening of a much weaker current is accompanied by a strong contraction.

But under certain circumstances a constant current flowing through a motor nerve may stimulate not only at the moment of closing, but during the entire period of closure. This happens for example with frog's nerves when the latter are taken from frogs which have been kept for a long time at a temperature below 10° C. (v. Frey); also with the nerves of warm-blooded animals when the current is not too weak. Again, if a constant current has been flowing through a nerve for a sufficient time, on opening the current there often appears a prolonged contraction instead of a simple short contraction. This continued state of contraction is often spoken of as "*Ritter's tetanus.*" Often also after the summit of the closing contraction has been passed, a cross-striated muscle does not recover its natural length immediately, but remains more or less shortened ("*Wundt's tetanus*"), and only returns to its resting condition when the current is broken—i. e., in case no opening contraction occurs. If the stimulus is very weak, the constant excitation is only a local one, spreading over a limited portion of the muscle. Finally, when a constant current is applied to an afferent nerve, a distinct sensation is felt during the entire period of closure, even when the peripheral end organs are excluded (Grützner, Langendorff, Biedermann).

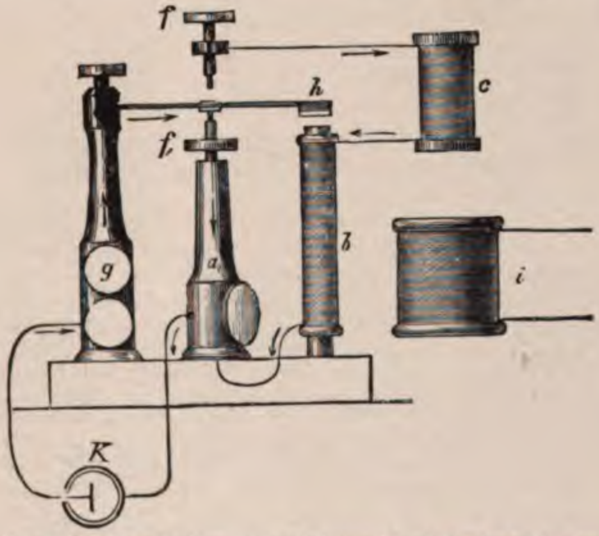

FIG. 159.—Details of the Wagner hammer or interrupter of the induction coil. *c*, primary coil; *i*, secondary coil. The primary current is generated in the battery *K* and the secondary or induced currents are led off by electrodes attached to the ends of the secondary coil.

We find therefore so many exceptions to Du Bois-Reymond's law, that in its original form it can no longer be regarded as of general application, although, so far as muscle alone is concerned, the excitation of large masses appears to depend upon sudden changes at the place of direct stimulation. Moreover, the law must take into account the *nature of the irritable tissue*:

the more irritable it is, the more do the visible phenomena of continuous excitation remain in the background, whereas the effects of variation in the current become the more apparent (Biedermann).

For all irritable tissues there is a minimum duration of the electric current necessary to give a stimulus. Other things being equal, the more this time is shortened, the less becomes the stimulating effect until finally it fails altogether. The length of time necessary to produce the maximal effect depends primarily on the strength of the current. The greater the strength the shorter the time may be. A constant current of medium strength requires 0.016 second to produce its maximal effect on motor nerves (J. König); no contractions are obtained if the time be reduced below 0.002 second. Induction shocks are still shorter than this; nevertheless, because of their high tension they are the most effective stimuli for the nerves.

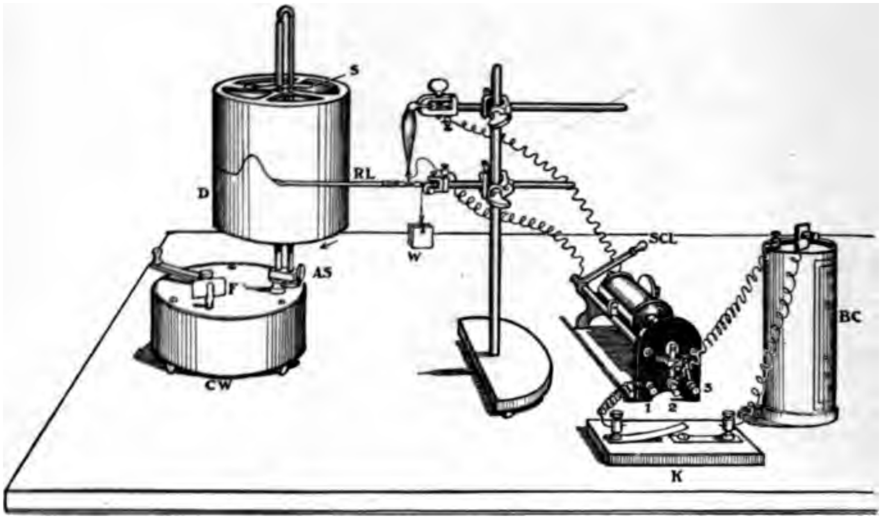

Fig. 160.—A convenient arrangement of the apparatus for sending induction shocks through a muscle is shown in this Figure. *BC*, the battery cell; *K*, key for closing and opening the primary current. When the wires are connected with binding posts 1 and 2 of the induction coil, single make and break shocks are obtained from the secondary coil and are conveyed by the wires connected therewith to the muscle. When the wires are connected with binding posts 1 and 3 of the induction coil the automatic interrupter is brought into play and a series of rapidly repeated (tetanic) shocks is obtained. By means of *hand electrodes* connected with the secondary end of the induction coil, stimuli may be applied in various other ways.

So far we have considered only the effects of currents suddenly turned on in their full strength. It is possible also by means of special apparatus to arrange the experiment so that starting from *nil* the current will increase gradually and only reach its maximum after a certain measured time. When this measured time does not exceed $\frac{1}{5000}$th of a second the effect is the same as that of a current of equal intensity suddenly opened in full force. When it is more than $\frac{1}{500}$th of a second the effect varies with the intensity of the current, being for a weak current less effective than the sudden opening, and with a strong current more effective (Gildemeister). But the most characteristic thing about these "time stimuli," as they are called, is that the contractions which they induce continue for a noticeably longer time, and the nerves and muscles can therefore be thrown by them into a state of excitation which lasts longer, than is the case with the sudden stimuli. This peculiarity, as we shall see later, is of great importance for the theoretical explanation of voluntary muscular contraction.

The nature of the irritable tissue again has much to do with the length of time required to stimulate it: the more slowly it reacts, the longer must the stimulus act to produce a visible effect.

A single induction shock, which is so effective for the nerve, is but slightly effective for smooth muscles. In certain stages of degeneration the skeletal muscles exhibit a very much reduced or even absolute lack of sensitivity toward induction currents, whereas their excitability to constant currents remains unimpaired or may even be increased (Erb). With the rapidly contracting frog's muscles, stimulation of the nerve by the break-induction shock is much stronger than by the make-induction shock, because the former is a more sudden stimulus. Nerve-muscle preparations of the turtle, which are much more sluggish in their action, behave in exactly the reverse manner.

3. *Law of Contraction.*—The stimulating effect of the constant current depends not only upon the strength but also upon the direction of the current in the nerve. If the current is weak it generally produces a contraction only when it is closed, no difference in which direction it is flowing. If the current is increased in strength (*medium current*), contractions occur also when it is opened, whether the current is flowing toward the muscle (*descending*) or away from it (*ascending*), although opening contractions do not always appear with the same strength of current in the two cases. Increasing the strength still more (*strong current*) we find that with the ascending current the closing contraction gradually becomes smaller until it finally disappears, while the opening contraction continues at its maximum. With the descending current we find the reverse condition: the closing contraction remains at its maximum however strong the current be made, but the opening contraction becomes smaller and smaller as the strength increases, and not infrequently it disappears. However, the strength at which the closing contraction disappears, when the current is ascending, is not always the same. And sometimes when the current is descending the opening contraction does not disappear at all but persists at a certain minimal size.

These generalizations may be summarized in the following formula, known as Pflüger's law of contraction:

Strength of Current.		Ascending current.	Descending current.
Weak..	Closing	C	C
	Opening	O	O
Medium	Closing	C	C
	Opening	C	C
Strong.	Closing	O	C
	Opening	C	O or weak C

C = contraction; O = no contraction.

It will be understood that the terms *weak*, *medium*, and *strong* as applied to the current in this discussion do not designate any absolute values of the current, since what is medium current for one nerve-muscle preparation may be strong for another. The terms are purely relative to any given preparation.

This peculiar behavior of a nerve-muscle preparation to currents of different strength, which finds expression in the law of contraction, depends upon another law enunciated by Pflüger, namely, that a constant current has no stimulating action on the nerve between the poles, but acts only at the poles. *On closing the current the stimulus starts from the cathode, on opening from the anode.*

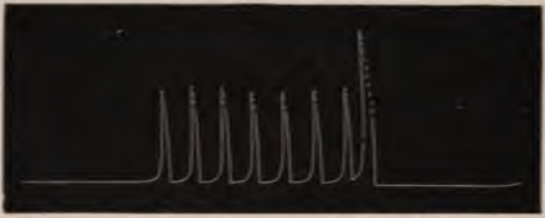

FIG. 161.—Catelectrotonus. The tracing is to be read from right to left. The nerve was first stimulated in the neighborhood of the cathode of the polarizing current with stimuli too weak to produce any effect while the polarizing current was not running. The polarizing current was then turned on, and, without changing the strength of the stimuli, they became effective. When the polarizing current was again turned off, the stimuli were again subminimal.

This *polar law of excitation* may be illustrated by the following experimental facts. If in stimulating with the constant current the electrodes be applied to the nerve as far apart as possible, and the latent period of the closing contractions be determined both for the ascending and descending currents, we find this period to be longer for the former than for the latter (v. Bezold). With the descending current the cathode is nearer the muscle than with the ascending current; hence the stimulus has a shorter distance to travel to reach the muscle with the former than with the latter. In a similar way it can be shown that the stimulus starts from the anode when the current is broken.

The *law of contraction* may be illustrated by carrying the experiment farther. Thus if from the determinations of the latent period just mentioned the rate of transmission of the stimulus be calculated, it will be found considerably lower than when it is determined on the same nerve, by the method (described on page 417) of stimulating at two points with the induction current. The reason is that with the ascending current the stimulus on its way to the muscle has experienced some resistance at the anode. This resistance varies considerably in amount according to the strength of the stimulating current. When the current is weak or of medium strength the stimulus at the cathode on closing the current is strong enough to overcome the resistance at the anode. But when the current is strong the resistance at the anode is too great to be overcome by the stimulus at the cathode, and it constitutes therefore a complete block. It can be shown also that when the cathode intervenes between the anode and the muscle, it creates a resistance to the anodic stimulus.

The polar law of excitation was deduced by Pflüger mainly on the ground of the alterations in excitability produced in the nerve by a constant current.

While the current is flowing the *excitability is increased* on both sides of the cathode; on both sides of the anode it is *decreased*. These alterations appear immediately (within 0.00007 second at most) after closing the current. In the intrapolar region there is found an indifferent point where the excitability of the nerve is not changed; and as the constant current increases in strength this point moves toward the cathode. At the same time the extrapolar alterations of excitability spread over greater lengths of the nerve.

Likewise during the first few moments after the current is opened alterations in the excitability appear, but they are just the reverse of those which occur while the current is closed—i. e., reduced at the cathode and increased at the anode.

These alterations may be studied in the following manner. A nerve is stimulated rhythmically, say once a second, with a current of constant strength, and the resulting contractions are recorded in the usual manner. If now while the stimulation is going on at the regular rhythm, a constant current be led into the nerve, and the stimuli fall in the neighborhood of the cathode of this current, the contractions at once become stronger; if they fall in the neighborhood of the anode, the contractions decrease in size and disappear altogether (see Figs. 161 and 162). When the current being led through the nerve is broken, contractions from stimuli applied at the cathode become smaller, those from stimuli at the anode become larger.

The increase of excitability at the cathode while the current is closed soon fails and passes over into a depressed condition, which, as Biedermann observes, is probably the expression of a local fatigue of the nerve.

The phenomena comprehended under the law of contraction may then be explained through the law of polar excitation as follows: *Weak currents* give a closing contraction because when the current is closed, the sudden rise in irritability of the nerve at the cathode is great enough to constitute a stimulus of itself. The stimulus is effective whether the current be ascending or descending, for in the one case the cathode is toward the muscle, and in the other the resistance at the anode, due to the decrease in irritability, is not great enough to block the stimulus. The sudden increase in excitability produced in the nerve at the anode when the current is broken is not yet sufficient to constitute a stimulus.—With the *medium current* the increase in excitability at the cathode on closing and at the anode on opening are both sufficient to produce a stimulus, and in neither case is the opposite pole strong enough to block it. The *strong current* is distinguished from the medium by the circumstance that while the current is closed the resistance at the anode is stronger than the excitation at the cathode and *vice versa* when the current is opened. Consequently with the ascending current the excitation started at the cathode cannot break through

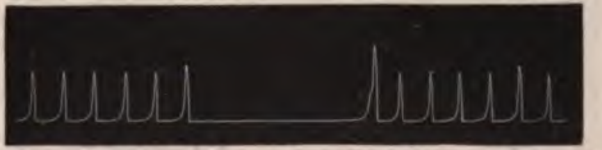

FIG. 162.—Anelectrotonus. The tracing to be read from right to left. A series of stimuli just strong enough to produce slight contractions were applied in the neighborhood of the anode for the polarizing current. When the polarizing current was turned on the stimuli became ineffective. When it was again turned off the stimuli again became effective.

the anode, and the closing contraction is wanting. With the descending current the excitation started at the anode meets with a resistance at the cathode which may or may not completely block it; hence the opening contraction either fails altogether or is greatly diminished.

Exactly the same laws hold for the *induction currents* as for the constant current. They also stimulate at the cathode as they appear and at the same time produce a resistance at the anode. When they are strong enough, they have a stimulating effect also as they disappear and then the stimulus starts from the anode.

The fact that the induction currents produce a resistance at their anode is demonstrated by the following experiment: a nerve is stimulated with ascending induction currents which, beginning with very weak shocks, are gradually increased in strength (Fig. 163). The height of the contractions at first increases, but after a time decreases, and with a certain strength the muscle remains at rest (Fig. 163; Nos. 11–18). If the strength of the shocks be raised still further, contractions appear again, which at first are weak (Nos. 19, 20), but gradually become stronger until they finally may become supramaximal. With a

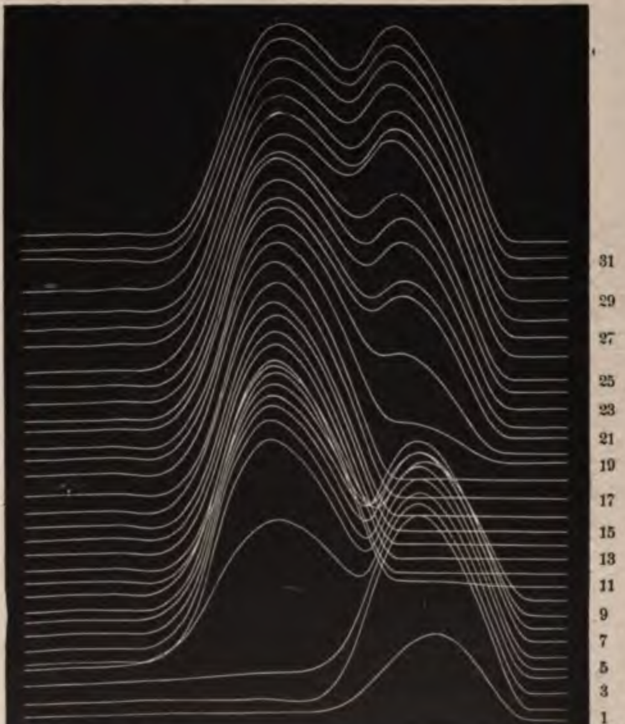

FIG. 163.—Stimulation of a nerve by a series of ascending make- and descending break-induction shocks of increasing strength. To be read from right to left. The first contraction of each pair was obtained by the ascending closing and the second by the descending opening shock. There are no "gaps" in the latter series.

series of shocks of increasing strength we have therefore a gap in the resulting contractions (Fick). This is only observed with the ascending currents, and is the result of a block at the anode. The absence of the contractions is therefore entirely analogous to the corresponding phenomena for the strong ascending constant current. The contractions coming after the gap and gradually increasing in size are produced really by the excitation taking place at the disappearance of the induction current, and are to be regarded for this reason as a sort of opening contractions. But further discussion of their nature here would carry us too far afield.

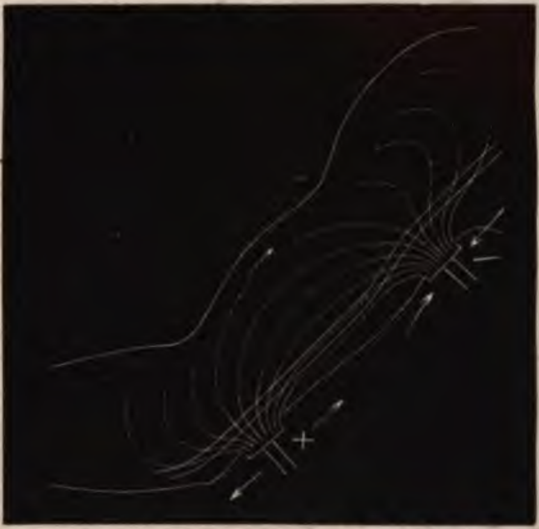

FIG. 164.—Schematic representation of the distribution of an electric current in a human arm on application of two electrodes over a nerve, after de Watteville.

The stimulating effects and the alterations of excitability produced by the electric current follow the same laws in human nerves as in the exsected frog's nerves (Waller and de Watteville).

In experiments on living men, the electrodes of course cannot be applied to the nerves themselves, but can only be placed on the skin; the nerve is stimulated then only by the threads of current which penetrate that far. It will be clear at once that the density of that portion of the current reaching a particular nerve will be greater the nearer the nerve lies to the surface of the skin. Consequently in using the current for therapeutic purposes the electrodes are applied to the skin at those points where the nerve, which it is desired to stimulate, can be reached most directly.

The effective anode is of course the place where the current enters the nerve itself, the effective cathode, the place where it leaves the nerve. If both poles were to be placed on the skin over the nerve, as in Fig. 164, anodes and cathodes would be present at almost every possible point along the nerve, as indicated by the radiating lines. Evidently such an experiment would not be adapted to the study of electrical effects on human nerves. The monopolar method is therefore used, the current being conveyed to and away from the body by electrodes

of different size, a large one (12 × 6 cm.) applied to the breast, and a small one (0.5–2 cm. diameter) applied over the motor point to be tested. Suppose now the large electrode is the anode: the current enters then with relatively low density, spreads out through the body with still less density and finally collects at the cathode with great density. Since now the effects of a current depend upon its density, it follows that with currents of moderate strength these effects will appear only at the smaller electrode. Some of the many threads of current reaching the smaller electrode from all parts of the body, will necessarily pass through the nerve under it. The effective cathode of the current lies where these threads pass out of the nerve, and if, as we have assumed, the smaller electrode is the cathode, other things being equal, the current will have its greatest possible density there. If the current is reversed so that it now enters the body by the smaller electrode (which is still over the nerve), the places where the threads of current leave the nerve constitute as before the effective cathode; the density of the current now however is less than in the first case (Fig. 165).

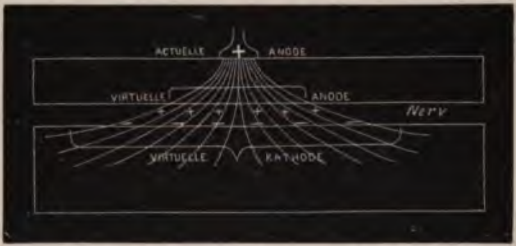

FIG. 165.—Schematic representation of the entrance into and exit from a nerve of a current applied to the skin over the nerve, after de Watteville.

The polar law of excitation applies also to muscle, both with the constant and induction current (v. Bezold, Engelmann, Biedermann; cf. page 416).

We have a very instructive proof of this in the "polar failure" of excitation discovered by Biedermann and Engelmann. If, for example, the end of a frog's sartorius muscle be narcotized and the cathode be applied to this injured place, on closing the current the muscle remains at rest. The normal muscle substance is not stimulated by the closure of a current as it passes from the normal to the paralyzed or dead muscle substance, and the mere passage of a current is not sufficient to discharge the contraction (Locke and Szymanowski). Similar phenomena may be shown on opening of the current when the anode is placed at the injured place.

E. EFFECT OF A RAPID SERIES OF STIMULI

If a nerve or a muscle be affected by two stimuli in rapid succession, so that the action resulting from the first has not yet come to an end when the second becomes effective, the relaxation which would otherwise follow the first contraction is interrupted and the effect of the second stimulus *is added to* the first; consequently the contraction of the muscle is greater than it commonly would be as the result of a single stimulus. It is only when the load of the muscle is very light that it contracts as strongly to a single stimulus as to rapidly repeated stimuli (v. Frey).

In *summated contractions* the ascending limb of the second contraction curve is steeper than that of the first, hence the summit of the second appears earlier than would be expected if its course were the same as the first (v. Kries). The latent period of the superimposed contraction is also said to be very much shorter than that following the first stimulus (Fick).

In order that successive stimuli may produce a summation they must not follow one another too rapidly. The smallest interval possible for any given preparation depends upon the temperature and the strength of the stimuli: for the nerves of the frog at ordinary room temperature it may be estimated at about 0.001 to 0.005 second. We have a *refractory period* therefore in nerves and skeletal muscles just as we have in heart muscle (cf. page 183).

If more than two stimuli affect the nerve or muscle at sufficiently short intervals the contraction of the muscle becomes still greater, and its curve is perfectly continuous, showing no separate summits (cf. Fig. 166). This form of contraction is called *tetanus*.

Complete tetanus appears only when the stimuli follow one another so rapidly that the interval between them is less than the time occupied by the active shortening of the muscle when that is maximal. The frequency depends therefore primarily upon the behavior of the muscle to single stimuli; the more rapidly a single contraction runs its course, the more frequently must the stimuli be given to produce complete tetanus. This is beautifully shown by the behavior of muscles of warm-blooded animals composed mainly of red or white fibers. The red *soleus* muscle of the rabbit falls into almost complete tetanus with ten stimuli per second, while the white *gastrocnemius medius* with the same frequency of stimulation gives very evident single contractions. A frequency of six stimuli per second permits the white muscle to relax almost completely

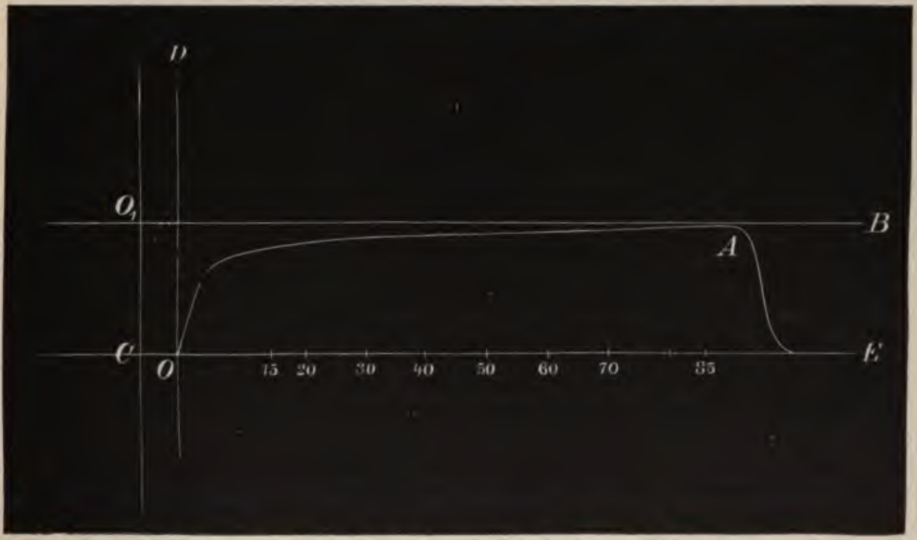

FIG. 166.—Tetanus curve of the frog's gastrocnemius, after Bohr. Twenty-seven stimuli per second.

between contractions, whereas it keeps the red muscle almost continuously contracted (Ranvier, Kronecker and Stirling; cf. Fig. 167).

Everything which tends to make the single contractions occupy more time operates to reduce the frequency of stimulation necessary to evoke complete tetanus. Thus fatigued muscles are thrown into tetanus with a lower frequency than unfatigued, because their contractions are slower.

The more the frequency is reduced below that which is just sufficient to produce tetanus, the more distinctly do the contractions produced by the individual stimuli stand out from one another, until finally below a certain frequency there is no fusion whatever. We have therefore all possible gradations between the isolated contractions and complete tetanus. This suggests that tetanus itself, notwithstanding the continuous curve by which it is represented graphically, is really a discontinuous process, and complete proof of this is furnished by the electrical variations accompanying tetanus (page 433).

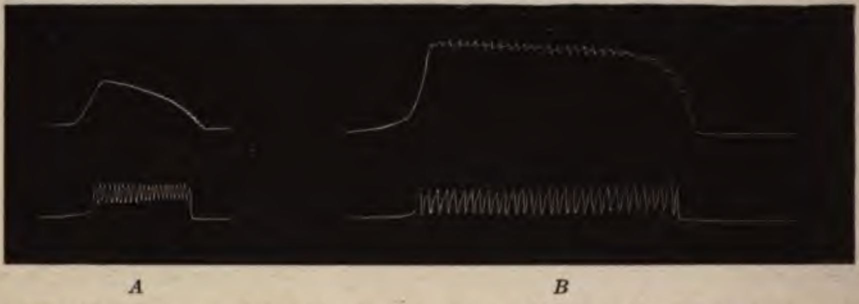

FIG. 167.—Tetanus curves of the white (lower tracings) and of the red (upper tracings) muscles of the rabbit, after Kronecker and Stirling. To be read from right to left. *A*, ten stimuli per second. *B*, six stimuli per second.

How are we to conceive of the processes going on in the muscle in tetanus? One significant fact is that by artificially supporting the muscle, so that it does not lift its weight until it has contracted some distance, the single contractions can be made to reach the same height as tetanus with the same strength of current (v. Frey). We may say, therefore, that in tetanus the muscle contracts to its utmost, because to a certain extent it is supported on itself. In addition to this the *irritability* of both nerve and muscle is increased by a previous stimulation—i. e., if the excitation is not too strong or does not continue so long as to involve much fatigue. Hence not infrequently it happens that stimuli, which of themselves are ineffective, become effective merely by being repeated with sufficient frequency.

Tetanus may be looked upon therefore as a sort of *heaping up* of small contractions due to the rapidity of the stimuli and to increased irritability.

F. VOLUNTARY CONTRACTIONS

If we compare voluntary contractions on the same drum with the rapid, twitchlike muscular contraction produced by a single artificial stimulus, we discover that the former are both *slower and less abrupt*. Comparing them with the contractions obtained by rapidly repeated shocks, we find more in common. Many other circumstances strongly support this resemblance, the most important of them being, that the voluntary contraction as well as the contractions which appear reflexly with strychnine poisoning are accompanied,

just as tetanus is, by action currents which signify a discontinuous excitation (Lovén). But it is worthy of note that the rhythm of these action currents in voluntary contractions, and others produced under the influence of the central nervous system, is only about half as rapid as the frequency of stimulation necessary to produce a complete tetanus. And yet the voluntary contraction as ordinarily recorded is quite continuous. This must be due to the fact that the single impulses sent out to the muscles from the central organs to produce a voluntary contraction last longer than the ordinary instantaneous stimuli (Lovén), and that the separate twitches are therefore more readily fused. We know, indeed, that a "time stimulus" (page 423) is longer drawn out than a momentary stimulus and that it is therefore better adapted to produce summation with a low frequency of stimulation.

The trembling of the muscles which accompanies a strained effort to overcome some great resistance or an attempt to hold a muscle contracted voluntarily to its utmost, are generally regarded as expressions of the individual impulses discharged from the central nervous system. The regulation of the innervating mechanisms would seem in these cases to be disturbed in some way so as to affect the fusion of the separate contractions. It has been shown that the number of such oscillations per second varies in man from seven or eight to twelve or thirteen (Lovén, v. Kries, Schäfer). The greatest muscular efforts are made, it appears, with a frequency of ten to twelve impulses per second.

§ 4. SIGNS OF ACTIVITY IN MUSCLE AND NERVE

A. ELECTRICAL PHENOMENA

1. *Action Current.*—The general law of the electrical variation known as the action current, which makes its appearance when nerve or muscle is active, has already been given on page 48. In view of its great importance for the general physiology of muscles and nerves, however, we must discuss it here somewhat more in detail.

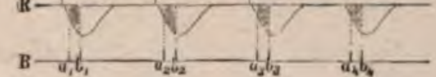

FIG. 168.—Schema illustrating a rheotome experiment.

In order to study time relations of the action current, one can use either the capillary electrometer whose excursions can be recorded by the photographic method, or the repeating rheotome of Bernstein.

Suppose we have an electrical variation of the form represented in Fig. 168. The galvanometer is too slow to reproduce this form correctly. But if we arrange the experiment so that a definite portion of each variation of the current—e. g., that included between a_1 and b_1 in Fig. 168—affects the galvanometer, and this is repeated many times, from the excursion of the galvanometer we can learn the extent of the electrical variation during this portion. If now we can determine in the same way the excursion of the galvanometer for the other

portions, say b_1 to c_1, c_1 to d_1, d_1 to e_1, etc., of course it will be possible to obtain the form of the entire variation. An apparatus which would enable us to make such determinations must permit of connection with the galvanometer at a definite moment after the beginning of the variation, and of breaking this connection at any desired moment during the variation. Since the electrical variation in muscles and nerves is started by the excitation, the requirements will be met if the galvanometer circuit can be closed or broken at any given interval after the instant of stimulation.

The *rheotome* of Bernstein (Fig. 169) consists of a wheel (*r*) revolving about a vertical axis, and carrying on its circumference three metal pegs, one of which (*c*) gives the stimulus to the nerve by closing or opening the primary current to an induction coil; the other two pegs insulated from the first, but in electrical connection with each other, serve to close and open the galvanometer circuit. At each revolution of the wheel the pegs c_1 and c_2 dip into the mercury troughs (q_1 and q_2) respectively which are connected with the muscle on the one hand and the galvanometer on the other. The mercury troughs are movable with respect to each other, so that the duration of the galvanometer current can be varied within wide limits. If now the wheel is revolved at a certain speed, with each revolution the muscle will receive a stimulus and the galvanometer circuit will be closed for a certain definite time after each stimulus. If we have the two contacts so arranged that the galvanometer is connected with the muscle at the same instant that the stimulus is given, the excursion of the galvanometer will represent the first part of the variation evoked by the stimulus. Then by shifting the contacts, the galvanometer can be connected at different intervals following the instant of stimulation until the entire variation is recorded.

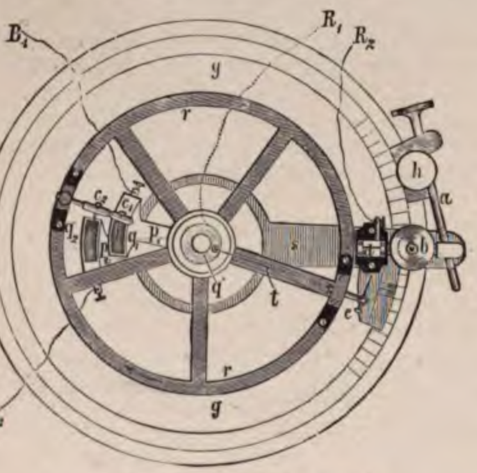

FIG. 169.—Rheotome of Bernstein.

If a muscle (or the heart) or a nerve be connected at two uninjured places (*a* and *b*, Fig. 170) with a galvanometer, and it be then stimulated at some outside point (*c*), the galvanometer shows that the point *a* situated nearer the point of stimulation becomes electrically negative to *b*, and then the current is reversed and *b* becomes negative to *a* (cf. pages 48 and 179). The *action current therefore consists of two phases*, each of which gives expression to the general law, that every active point of a muscle or nerve is electrically negative to every resting point (page 48). When the excitation spreads from the point *c*, the nearer of the two points naturally becomes active first, while the more distant point (*b*) is still resting; hence the first phase. When the excitation reaches the point *b* and the point *a* first stimulated has gradually passed into a resting state, the second phase appears.

The action current does not represent an artificial product, but is a process intimately connected with the process of excitation, for it is produced by all kinds of stimuli; it is propagated at the same rate of speed as the excitation and varies in strength to a certain extent with the strength of stimulation.

If the nerve or the muscle be led off to the galvanometer, not from two points on the longitudinal surface, but from the longitudinal surface and a cross section, the second phase of the action current no longer appears, but the current is now directed from the longitudinal surface over to the cross section. It was in this form that the action current was first discovered. Since it runs in the opposite direction from the current of rest (see page 48) it was designated by Du Bois-Reymond as the *negative variation* of the current of rest.

The action current is the only functional change which we have thus far been able to observe in living nerves. It is of great importance also for the reason that it permits us to determine the *nature of any muscular contraction.*

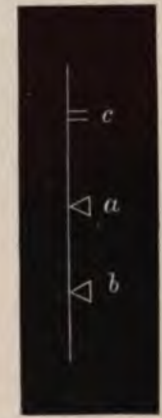

FIG. 170.—Schema illustrating spread of an excitation causing an action current.

We have already become acquainted with an example of this in studying the heart. The action current there showed us that, notwithstanding its long duration, the contraction of the heart is in reality a simple muscular twitch (cf. page 179).

There are other kinds of contractions, like tetanus and voluntary contractions, which as we have seen are apparently continuous, but which the action current proves to be discontinuous. If by the use of the rheotome, a muscle be stimulated often enough to produce complete tetanus, the excursions of the galvanometer will show that each separate stimulus produces a special action current of its own—i. e., every excitation causes a molecular change in the muscle, although the change may not be apparent in the mechanical behavior of the muscle.

The action current of muscle as well as of nerve is strong enough to have a stimulating action of its own (Matteucci). If the nerve of one muscle, B, be laid across the belly of another muscle, A, and the second muscle be then stimulated through its own nerve, with each contraction of A, B also contracts, and this even in case A is so tense that it no longer changes its form. The contractions of B agree minutely in number, strength and sequence with those of A. If A is tetanized, B also is tetanized. These phenomena are called *secondary contractions*, secondary tetanus, etc.

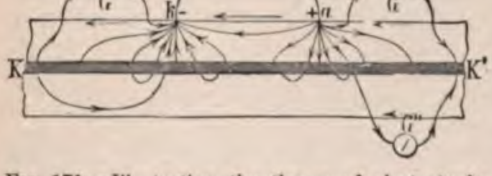

FIG. 171.—Illustrating the theory of electrotonic currents, after Hermann.

2. *Electrotonic Currents.*—When an electric current is conducted through a certain length of a medullated nerve and another portion of the nerve outside of this length is connected with the galvanometer, an

portions, say b_1 to c_1, c_1 to d_1, d_1 to e_1, etc., of course it will be possible to obtain the form of the entire variation. An apparatus which would enable us to make such determinations must permit of connection with the galvanometer at a definite moment after the beginning of the variation, and of breaking this connection at any desired moment during the variation. Since the electrical variation in muscles and nerves is started by the excitation, the requirements will be met if the galvanometer circuit can be closed or broken at any given interval after the instant of stimulation.

The *rheotome* of Bernstein (Fig. 169) consists of a wheel (r) revolving about a vertical axis, and carrying on its circumference three metal pegs, one of which (c) gives the stimulus to the nerve by closing or opening the primary current to an induction coil; the other two pegs insulated from the first, but in electrical connection with each other, serve to close and open the galvanometer circuit. At each revolution of the wheel the pegs c_1 and c_2 dip into the mercury troughs (q_1 and q_2) respectively which are connected with the muscle on the one hand and the galvanometer on the other. The mercury troughs are movable with respect to each other, so that the duration of the galvanometer current can be varied within wide limits. If now the wheel is revolved at a certain speed, with each revolution the muscle will receive a stimulus and the galvanometer circuit will be closed for a certain definite time after each stimulus. If we have the two contacts so arranged that the galvanometer is connected with the muscle at the same instant that the stimulus is given, the excursion of the galvanometer will represent the first part of the variation evoked by the stimulus. Then by shifting the contacts, the galvanometer can be connected at different intervals following the instant of stimulation until the entire variation is recorded.

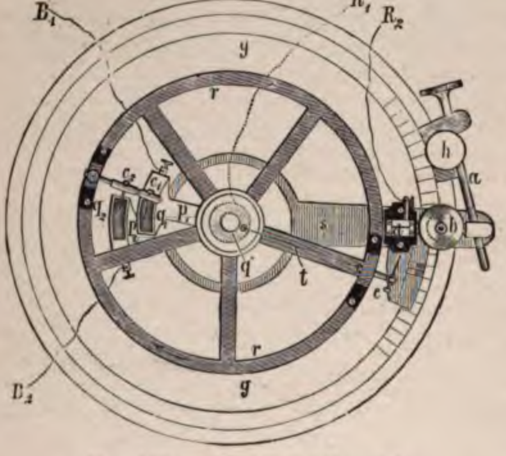

Fig. 169.—Rheotome of Bernstein.

If a muscle (or the heart) or a nerve be connected at two uninjured places (a and b, Fig. 170) with a galvanometer, and it be then stimulated at some outside point (c), the galvanometer shows that the point a situated nearer the point of stimulation becomes electrically negative to b, and then the current is reversed and b becomes negative to a (cf. pages 48 and 179). The *action current therefore consists of two phases*, each of which gives expression to the general law, that every active point of a muscle or nerve is electrically negative to every resting point (page 48). When the excitation spreads from the point c, the nearer of the two points naturally becomes active first, while the more distant point (b) is still resting; hence first phase. When the excitation reaches the point b and the point a stimulated has gradually passed into a resting state, the second appears.

D. MECHANICAL WORK

The amount of mechanical work done by a muscular contraction depends primarily upon the strength of the stimulus, and upon the load.

1. *Effect of the Strength of Stimulus.*—If a muscle bearing a constant load be stimulated with a graded series of shocks beginning at a very low level and increasing slowly, it is found, both with direct electrical stimulation of the muscle and with mechanical or electrical stimulation of the nerve, that the height of the contractions increases more and more slowly with a uniform increase in the strength of the stimuli, and that it finally approaches its maximum after the manner of an asymptote (Fig. 172). The maximum shortening which can be obtained under the most favorable circumstances with a single contraction is about twenty per cent of the natural length of the muscle.

The muscular tension obtained with a maximal stimulus applied to the nerve is considerably smaller than that obtained by a maximal stimulus applied directly to the muscle itself (Dean). If this is true of the natural stimulation from the central nervous system also, it means that the muscles are always capable of more work than can ever, under normal circumstances, be obtained from them.

2. *Effect of Load with Constant Stimulus.*—We shall consider only the case of a maximal stimulus.

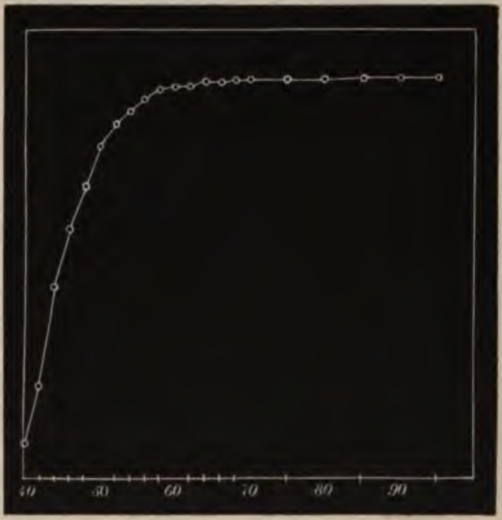

FIG. 172.—Frog's gastrocnemius. Stimulation of the nerve with break-induction shocks; load constant. The abscissæ represent the strength of the stimuli, the ordinates the height of the contractions.

One can vary the way in which the power of the muscle is taken up by making the contraction: (1) *isotonic*—i. e., where the load is constant throughout the contraction; (2) *auxotonic*, where the load increases constantly throughout; and (3) by *supporting the load* so that it is not lifted until the muscle has contracted a certain distance (after-loading).

A perfect *isotonic contraction* is probably never obtained. Even when the mechanical conditions of the experiment fulfill the requirements for isotony as completely as possible, the contraction is retarded at its beginning by the inertia of the masses to be moved, consequently the tension of the muscle is greater at the start than later.

We designate as *auxotonic contractions*, first those in which the muscle works against a stiff spring, where the tension naturally increases as long as the muscle continues to contract, and secondly, those contractions in which the tension of the muscle is purposely increased by retardation of the movement at its beginning. Here belong the so-called *simple projectile motion* (Helmholtz), in which the muscle lifts a weight fastened directly to its free end, and the *projectile motion with dead weights* (Fick), where the muscle pulls on a lever with balanced weights.

In Figs. 173 and 174 are given examples of some of the different forms of motion, namely: Fig. 173 *a*, an isotonic contraction, Fig. 173 *b*, a simple projectile motion, Fig. 174, projectile motions with dead balanced weights.

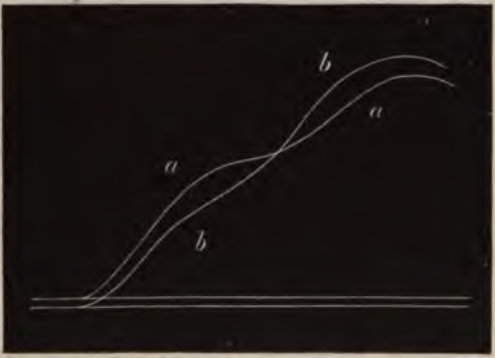

FIG. 173.—Frog's gastrocnemius. *a*, isotonic contraction; *b*, simple projectile contraction. Both were obtained with the same loads, 80 g., after Santesson.

In curves approximately isotonic, Fig. 173 *a*, as well as in pure auxotonic curves, which naturally reproduce the changes in length of the muscle most exactly, we find in the ascending limb a break, which is not an artifact but which, on grounds that cannot be discussed here, is probably due to the more sluggish contraction of the red muscle fibers (cf. page 416). In the projectile curve this irregularity does not appear, at least not so clearly, because the movement of the lever does not record the finer details of the contraction. The contraction produced by a single stimulus is, therefore, to a certain extent compound, owing to the fact that the different kinds of fibers composing the muscle become active at different times. In an exact analysis of muscular contractions, it is necessary to give this circumstance its proper weight.

Fig. 175 represents the single contraction of a muscle poisoned with veratrin, recorded on a slow-moving drum. Veratrin affects the red muscle fibers so that they contract much more slowly than is normal. The first rapid curve is referable to the white fibers, the second long-drawn-out curve to the red fibers.

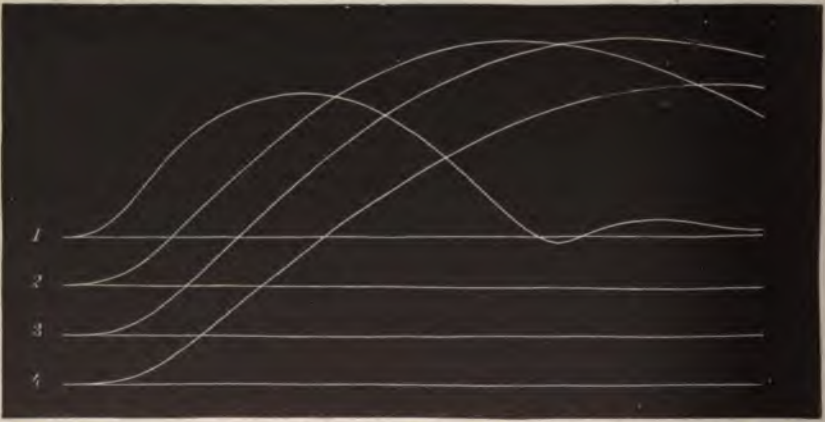

FIG. 174.—Frog's gastrocnemius. 1, loaded with 4 g., i. e., with the bare lever; 2, 40 g. dead weight; 3, 100 g. dead weight; 4, 200 g. dead weight.

After these preliminary remarks we can proceed with the discussion of the *effect of load* on the work of a muscle. We can say in general that the height of the contraction is less the greater the load. But this rule cannot stand without qualification. For under the isotonic arrangement we find the height less with a very light load than it is with one somewhat heavier (v. Frey), and under the purely auxotonic arrangement the height increases with the load up to a fairly high primary tension. Moreover, even if the height of the contraction does decrease as the load increases, it does so much more slowly than the load increases; so that up to a certain limit the work done (product of the load by the height of contraction) is greater, the greater the load (E. F. Weber).

Again, *an increase in the tension* of a muscle during its contraction has a decidedly favorable effect on its performance. Under some circumstances the contractions against a stiff spring are just as high or even higher than isotonic contractions obtained with a primary tension of the same amount (Santesson); and projectile contractions are sometimes higher than isotonic contractions with the same primary tension (cf. Fig. 173). Finally, cases have been recorded where auxotonic contractions which begin with the same tension are higher with a strong spring than with a weak one. We can say, therefore, that within certain limits the work done by a muscle is increased both by a higher primary tension and by an increase in the tension during the contraction.

In close connection with this comes the additional fact that under the isometric arrangement the increase in tension takes place much more rapidly than does the shortening under the so-called isotonic arrangement; or, in other words, its length remaining the same, the muscle reaches its maximum tension much earlier than it reaches its maximum shortening when the tension remains the same (Fick, Fig. 176).

A muscle appears therefore to have the *power of regulating the amount of work done* under a given stimulus, according to the requirements of the case. We must forego a complete theoretical discussion of these facts here; but we would direct attention to the significance of the red fibers in this connection. They are, as it appears, the most important source of the additional work done as the result of an increased tension. Thus we find that the secondary lift due to these fibers, in contractions against a tense spring in-

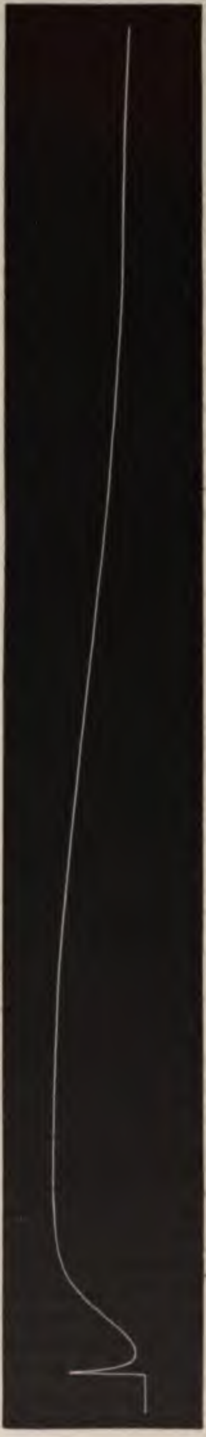

Fig. 175.—Contraction curve of a frog's gastrocnemius poisoned with veratrin, after Santesson.

of different size, a large one (12 × 6 cm.) applied to the breast, and a small one (0.5–2 cm. diameter) applied over the motor point to be tested. Suppose now the large electrode is the anode: the current enters then with relatively low density, spreads out through the body with still less density and finally collects at the cathode with great density. Since now the effects of a current depend upon its density, it follows that with currents of moderate strength these effects will appear only at the smaller electrode. Some of the many threads of current reaching the smaller electrode from all parts of the body, will necessarily pass through the nerve under it. The effective cathode of the current lies where these threads pass out of the nerve, and if, as we have assumed, the smaller electrode is the cathode, other things being equal, the current will have its greatest possible density there. If the current is reversed so that it now enters the body by the smaller electrode (which is still over the nerve), the places where the threads of current leave the nerve constitute as before the effective cathode; the density of the current now however is less than in the first case (Fig. 165).

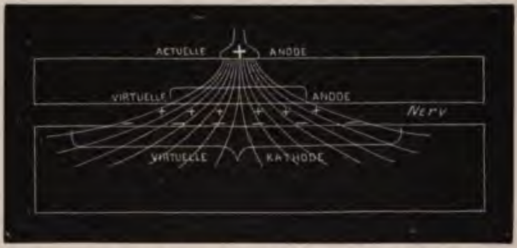

FIG. 165.—Schematic representation of the entrance into and exit from a nerve of a current applied to the skin over the nerve, after de Watteville.

The polar law of excitation applies also to muscle, both with the constant and induction current (v. Bezold, Engelmann, Biedermann; cf. page 416).

We have a very instructive proof of this in the "polar failure" of excitation discovered by Biedermann and Engelmann. If, for example, the end of a frog's sartorius muscle be narcotized and the cathode be applied to this injured place, on closing the current the muscle remains at rest. The normal muscle substance is not stimulated by the closure of a current as it passes from the normal to the paralyzed or dead muscle substance, and the mere passage of a current is not sufficient to discharge the contraction (Locke and Szymanowski). Similar phenomena may be shown on opening of the current when the anode is placed at the injured place.

E. EFFECT OF A RAPID SERIES OF STIMULI

If a nerve or a muscle be affected by two stimuli in rapid succession, so that the action resulting from the first has not yet come to an end when the second becomes effective, the relaxation which would otherwise follow the first contraction is interrupted and the effect of the second stimulus *is added to* the first; consequently the contraction of the muscle is greater than it commonly would be as the result of a single stimulus. It is only when the load of the muscle is very light that it contracts as strongly to a single stimulus as to rapidly repeated stimuli (v. Frey).

In *summated contractions* the ascending limb of the second contraction curve is steeper than that of the first, hence the summit of the second appears earlier than would be expected if its course were the same as the first (v. Kries). The latent period of the superimposed contraction is also said to be very much shorter than that following the first stimulus (Fick).

In order that successive stimuli may produce a summation they must not follow one another too rapidly. The smallest interval possible for any given preparation depends upon the temperature and the strength of the stimuli: for the nerves of the frog at ordinary room temperature it may be estimated at about 0.001 to 0.005 second. We have a *refractory period* therefore in nerves and skeletal muscles just as we have in heart muscle (cf. page 183).

If more than two stimuli affect the nerve or muscle at sufficiently short intervals the contraction of the muscle becomes still greater, and its curve is perfectly continuous, showing no separate summits (cf. Fig. 166). This form of contraction is called *tetanus*.

Complete tetanus appears only when the stimuli follow one another so rapidly that the interval between them is less than the time occupied by the active shortening of the muscle when that is maximal. The frequency depends therefore primarily upon the behavior of the muscle to single stimuli; the more rapidly a single contraction runs its course, the more frequently must the stimuli be given to produce complete tetanus. This is beautifully shown by the behavior of muscles of warm-blooded animals composed mainly of red or white fibers. The red *soleus* muscle of the rabbit falls into almost complete tetanus with ten stimuli per second, while the white *gastrocnemius medius* with the same frequency of stimulation gives very evident single contractions. A frequency of six stimuli per second permits the white muscle to relax almost completely

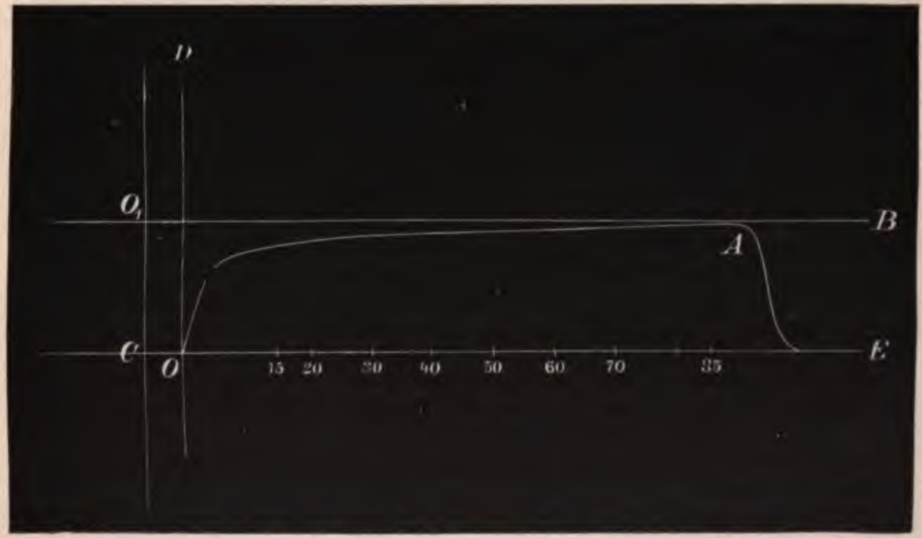

Fig. 166.—Tetanus curve of the frog's gastrocnemius, after Bohr. Twenty-seven stimuli per second.

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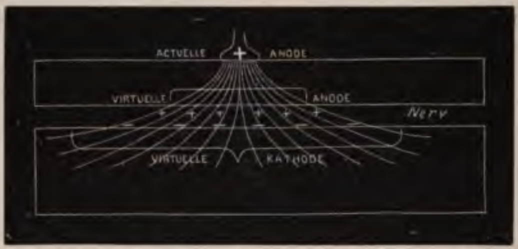

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partial contraction. There can be no doubt that such partial contractions occur also normally under the influence of the nervous system, although probably with still nicer gradations. In this way the activity of the muscle is adapted to the work to be performed. If no great degree of tension is called for, only a few muscle fibers contract, the others remain quiet and do not become fatigued. Since on the other hand the extent of the contraction does not depend upon the cross section, but upon the length of the muscle, we may get just as much shortening with a partial contraction as when the whole muscle is active.

§ 6. FATIGUE AND RECOVERY OF MUSCLES AND NERVES

A. GENERAL PHENOMENA

If a *frog's muscle* be stimulated repeatedly with single shocks given every one to two seconds, at first its contractions increase in size, even if the stimulus remain of the same strength ("treppe" of Bowditch and Buckmaster), and then they gradually decrease until complete exhaustion is reached. From the first of the series the contractions become more prolonged, since both the ascending and the descending limbs of the curve, but especially the latter, occupy more time. As fatigue progresses and the longer stimulation is kept up, there gradually develops a new condition of the muscle: at the end of the contraction it does not return to its resting position but remains more and more shortened.[1] The muscle finally becomes a sluggish, stubborn mass yielding to the traction which strives to restore it to its original form, with extreme slowness (Funke). In the series represented in Fig. 177 a muscle kept perfused with blood was stimulated every 1.5 seconds. Only the first ten of every fifty contractions are here reproduced, the six series representing all told some three hundred separate movements. When the interval between stimuli is made still shorter, say 0.5 second, as fatigue continues the descending limb of the curve does not reach the base line, before it is met by the following stimulus, and the curve becomes much like an incomplete tetanus. With a longer interval, say six seconds, the contraction is not prolonged, or only slightly so, and the reduction in the height of the curve is the only expression of fatigue.

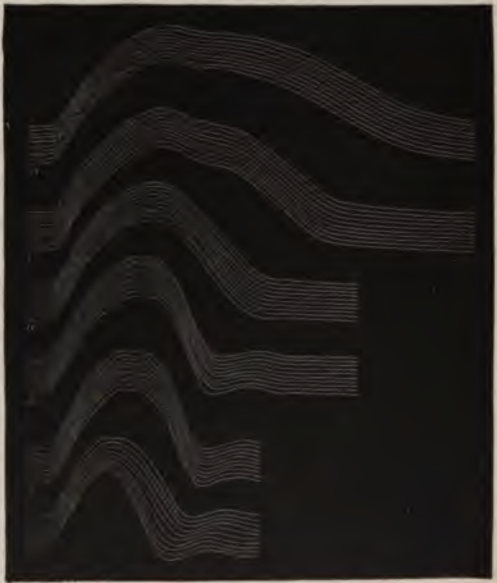

FIG. 177.—Changes in the character of the contraction produced by fatigue, after Rollet.

The *muscle of warm-blooded animals*, kept perfused with blood, show, according to Rollet, only this latter form of fatigue, with no material increase in the duration of the contraction even when the interval between stimuli is very

of different size, a large one (12 × 6 cm.) applied to the breast, and a small one (0.5–2 cm. diameter) applied over the motor point to be tested. Suppose now the large electrode is the anode: the current enters then with relatively low density, spreads out through the body with still less density and finally collects at the cathode with great density. Since now the effects of a current depend upon its density, it follows that with currents of moderate strength these effects will appear only at the smaller electrode. Some of the many threads of current reaching the smaller electrode from all parts of the body, will necessarily pass through the nerve under it. The effective cathode of the current lies where these threads pass out of the nerve, and if, as we have assumed, the smaller electrode is the cathode, other things being equal, the current will have its greatest possible density there. If the current is reversed so that it now enters the body by the smaller electrode (which is still over the nerve), the places where the threads of current leave the nerve constitute as before the effective cathode; the density of the current now however is less than in the first case (Fig. 165).

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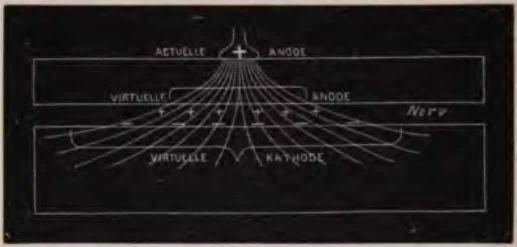
[1] This condition is called contracture.—ED.



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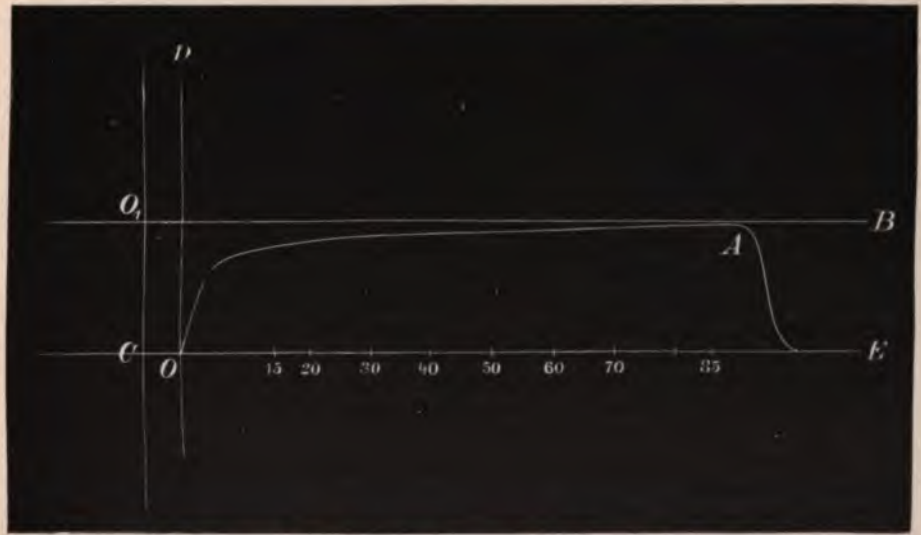

FIG. 166.—Tetanus curve of the frog's gastrocnemius, after Bohr. Twenty-seven stimuli per second.

able to lift the load; but if the load be diminished, he can continue the work immediately. The fatigue curve either declines rapidly at first and more slowly at the end, as in Fig. 180, A, or the fall at the beginning is slight and is rapid toward the end (Fig. 180, B). Judging by Mosso's results every individual has his own peculiar form of fatigue curve.

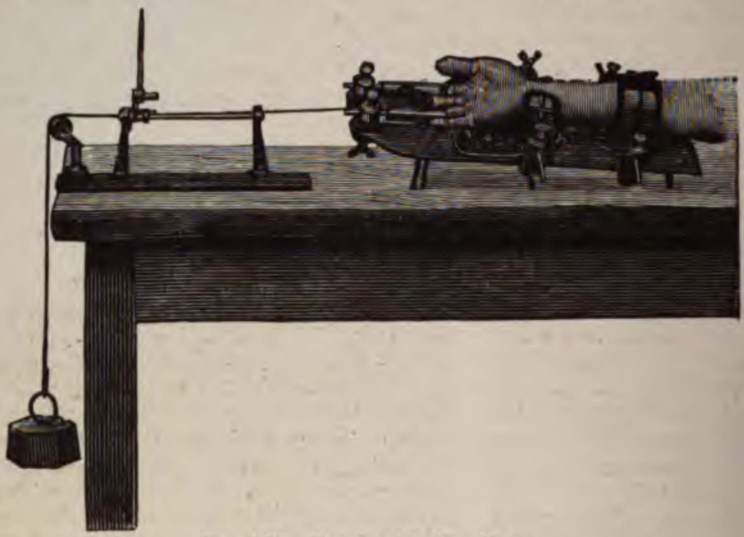
Fig. 179.—Ergograph, after Mosso.

Of the factors which influence the progress of fatigue we shall investigate first the effect of frequency of contraction with a constant load. Figs. 181, A to

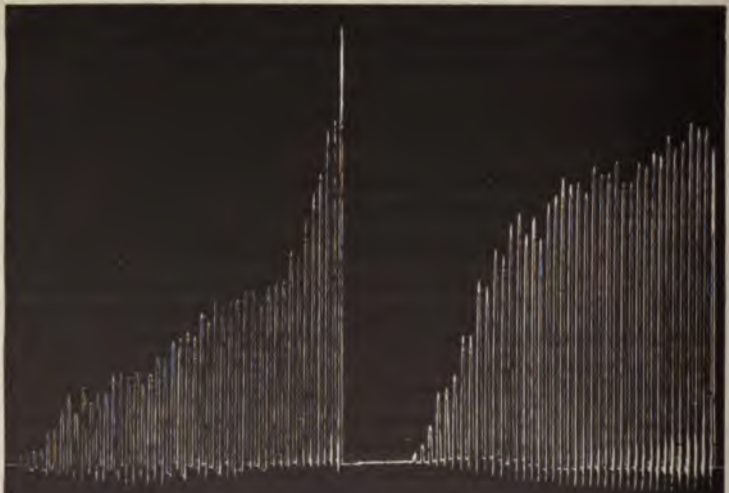

Fig. 180.—Fatigue tracings obtained with the ergograph of Mosso. To be read from right to left.

D show that exhaustion comes on more rapidly the smaller the interval between contractions. In Fig. 181, A we find only fourteen contractions before complete exhaustion, mechanical work = 0.912 kg. m. In Fig. 181, B the number of contractions is eighteen, and the mechanical work done 1.080 kg. m. In Fig. 181, C the number of contractions is thirty-one and the mechanical work 1.842 kg. m. With a rhythm of one contraction every ten seconds no fatigue at all appears (Fig. 181, D). An interval of ten seconds, therefore, is sufficient to permit a skeletal muscle to recover completely.

When a muscle is worked at a rapid rhythm to the point of complete exhaustion, it requires a rather long time to recover completely—in the experiments of Maggiora from one and one-half to two hours. It was also shown in these experiments that the last contractions of a series ending in complete exhaustion, are the most fatiguing. If only the first part, say the first fifteen contractions, of a fatigue series be carried out and rest be then permitted, the muscle will recover in a much shorter time proportionally than if it were completely fatigued. Consequently the total amount of work which can be done in a day is considerably greater if the muscles be not pushed at any time to the limit of their powers. For example, a muscle making fifteen contractions every thirty minutes for fourteen hours did mechanical work of 26.9 kg. m.; the same muscle when made to perform the whole series of fatigue curves every two hours accomplished a mechanical work of only 14.7 kg. m.; a difference of 12.2 kg. m.

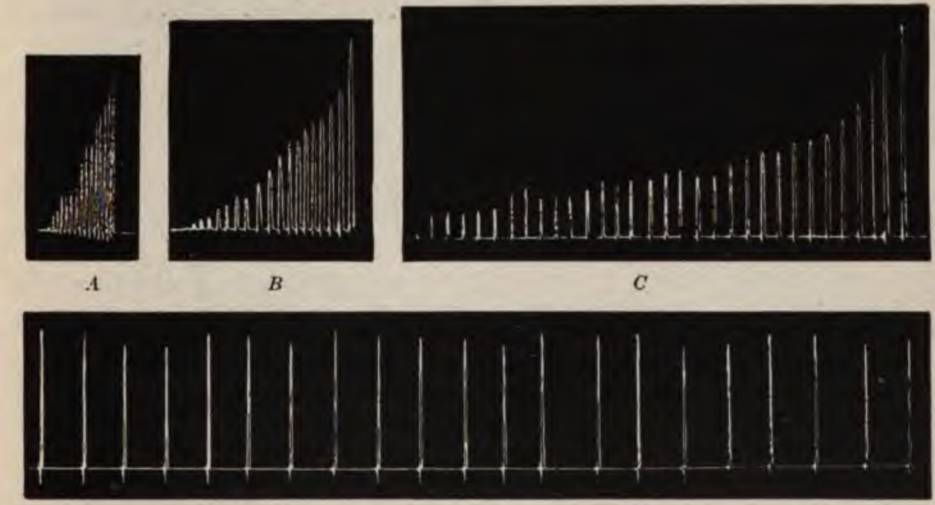

FIG. 181.—The onset of fatigue under stimuli of the same strength, given at different intervals, after Maggiora. *A*, once a second; *B*, once every two seconds; *C*, once in four seconds; *D*, once in ten seconds. To be read from right to left.

Anæmia, fasting, want of sleep, among other things, reduce the working power, and favor the onset of fatigue. The capability of work is increased, on the other hand, by rest, by taking food, and by massage—the latter even in case the muscle be previously not fatigued. The effect of massage after work therefore consists not only in the removal of products arising from the expenditure of energy, but also, and to a considerable extent, in the more active circulation of the blood and lymph and possibly in some alteration of metabolism

the anode, and the closing contraction is wanting. With the descending current the excitation started at the anode meets with a resistance at the cathode which may or may not completely block it; hence the opening contraction either fails altogether or is greatly diminished.

Exactly the same laws hold for the *induction currents* as for the constant current. They also stimulate at the cathode as they appear and at the same time produce a resistance at the anode. When they are strong enough, they have a stimulating effect also as they disappear and then the stimulus starts from the anode.

The fact that the induction currents produce a resistance at their anode is demonstrated by the following experiment: a nerve is stimulated with ascending induction currents which, beginning with very weak shocks, are gradually increased in strength (Fig. 163). The height of the contractions at first increases, but after a time decreases, and with a certain strength the muscle remains at rest (Fig. 163; Nos. 11–18). If the strength of the shocks be raised still further, contractions appear again, which at first are weak (Nos. 19, 20), but gradually become stronger until they finally may become supramaximal. With a

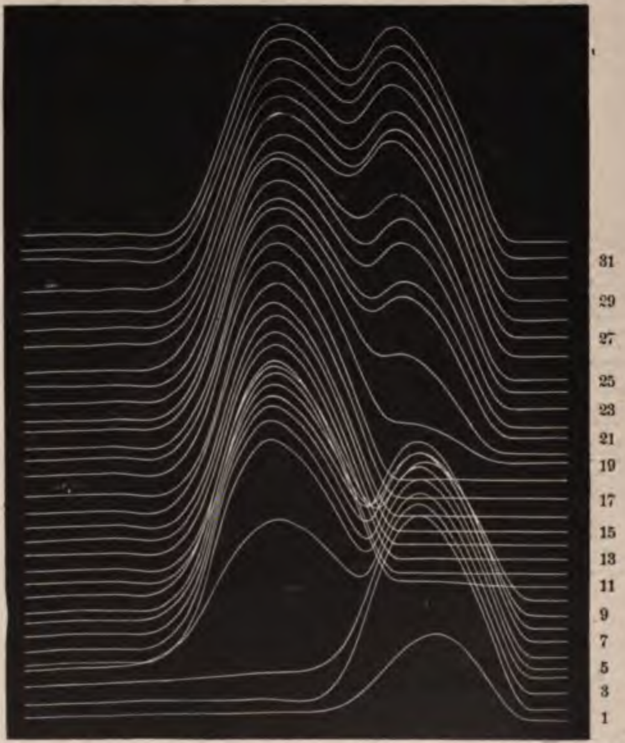

FIG. 163.—Stimulation of a nerve by a series of ascending make- and descending break-induction shocks of increasing strength. To be read from right to left. The first contraction of each pair was obtained by the ascending closing and the second by the descending opening shock. There are no "gaps" in the latter series.

The following table, compiled by Blix, contains some data on the maximal muscular capacity of man at different kinds of work:

KIND OF WORK.	Time.	Kg. m. per second.	Observer.
Climbing mountain and stairs...	8 hours	10.5	Weissbach
Turning crank	1¼ hours	12.5	Sjöstrom
" "	15 minutes	17.0	"
" "	5 minutes	19.5	"
" "	1¼ hours	27.7	"
Climbing stairs without load....	4 seconds	101.2	Blix
Climbing stairs with load.......	4.5 seconds	95.4	"

It is evident that the capacity for work calculated per second is greater, the shorter the total time occupied. The highest record of endurance yet made was observed in a six-day bicycle contest in New York. According to Atwater's calculation the victor performed during his first day of twenty-three hours and ten minutes an average of 25 kg. m. per second, and in the whole time, one hundred and eight hours and forty-four minutes, an average of 20.2 kg. m. per second.

§ 7. RIGOR MORTIS

A muscle cut out of the body or excluded from the circulation passes sooner or later (ten minutes to several hours) into a rigid condition known as the death stiffening or *rigor mortis.* It is now shorter, thicker and firmer, turbid, opaque and less extensible; its reaction is acid, probably owing to the transformation of a portion of the diphosphates into monophosphates brought about by the lactic acid formed.

Rigor of muscle is produced also by warming to 48°–50° C., by the effects of distilled water, by acids and by various other substances. It appears more readily after heavy muscular work than otherwise, but on the other hand appears later if the muscle has been paralyzed by section of its nerve. Rigor mortis is the cause of the rigidity of the body after death. Under certain circumstances, which have not yet been successfully imitated, the stiffening comes on immediately after death, so that the body becomes fixed in the position it had at the instant of death.

Rigor is regarded by most authors as *coagulation* of the muscle proteids. But the processes taking place in rigor are only partially explained in this way, for we do not even know definitely how the proteids obtainable from muscle plasma occur in the living muscle. Besides, the phenomena of coagulation in a muscle extract, and the rigidity brought about artificially by different reagents, present several points of difference from the natural death stiffening.

§ 8. SMOOTH MUSCLES

The most satisfactory smooth muscles for study are those whose fibers run parallel, like the *retractor penis* of the dog and the circular muscles in the stomach of the frog. The extensibility of such muscles is relatively great and the elastic after-effect is very considerable. A small weight acting for a long time

of different size, a large one (12 × 6 cm.) applied to the breast, and a small one (0.5–2 cm. diameter) applied over the motor point to be tested. Suppose now the large electrode is the anode: the current enters then with relatively low density, spreads out through the body with still less density and finally collects at the cathode with great density. Since now the effects of a current depend upon its density, it follows that with currents of moderate strength these effects will appear only at the smaller electrode. Some of the many threads of current reaching the smaller electrode from all parts of the body, will necessarily pass through the nerve under it. The effective cathode of the current lies where these threads pass out of the nerve, and if, as we have assumed, the smaller electrode is the cathode, other things being equal, the current will have its greatest possible density there. If the current is reversed so that it now enters the body by the smaller electrode (which is still over the nerve), the places where the threads of current leave the nerve constitute as before the effective cathode; the density of the current now however is less than in the first case (Fig. 165).

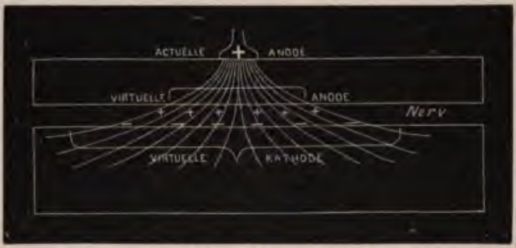

FIG. 165.—Schematic representation of the entrance into and exit from a nerve of a current applied to the skin over the nerve, after de Watteville.

The polar law of excitation applies also to muscle, both with the constant and induction current (v. Bezold, Engelmann, Biedermann; cf. page 416).

We have a very instructive proof of this in the "polar failure" of excitation discovered by Biedermann and Engelmann. If, for example, the end of a frog's sartorius muscle be narcotized and the cathode be applied to this injured place, on closing the current the muscle remains at rest. The normal muscle substance is not stimulated by the closure of a current as it passes from the normal to the paralyzed or dead muscle substance, and the mere passage of a current is not sufficient to discharge the contraction (Locke and Szymanowski). Similar phenomena may be shown on opening of the current when the anode is placed at the injured place.

E. EFFECT OF A RAPID SERIES OF STIMULI

If a nerve or a muscle be affected by two stimuli in rapid succession, so that the action resulting from the first has not yet come to an end when the second becomes effective, the relaxation which would otherwise follow the first contraction is interrupted and the effect of the second stimulus *is added to* the first; consequently the contraction of the muscle is greater than it commonly would be as the result of a single stimulus. It is only when the load of the muscle is very light that it contracts as strongly to a single stimulus as to rapidly repeated stimuli (v. Frey).

In *summated contractions* the ascending limb of the second contraction curve is steeper than that of the first, hence the summit of the second appears earlier than would be expected if its course were the same as the first (v. Kries). The latent period of the superimposed contraction is also said to be very much shorter than that following the first stimulus (Fick).

In order that successive stimuli may produce a summation they must not follow one another too rapidly. The smallest interval possible for any given preparation depends upon the temperature and the strength of the stimuli: for the nerves of the frog at ordinary room temperature it may be estimated at about 0.001 to 0.005 second. We have a *refractory period* therefore in nerves and skeletal muscles just as we have in heart muscle (cf. page 183).

If more than two stimuli affect the nerve or muscle at sufficiently short intervals the contraction of the muscle becomes still greater, and its curve is perfectly continuous, showing no separate summits (cf. Fig. 166). This form of contraction is called *tetanus*.

Complete tetanus appears only when the stimuli follow one another so rapidly that the interval between them is less than the time occupied by the active shortening of the muscle when that is maximal. The frequency depends therefore primarily upon the behavior of the muscle to single stimuli; the more rapidly a single contraction runs its course, the more frequently must the stimuli be given to produce complete tetanus. This is beautifully shown by the behavior of muscles of warm-blooded animals composed mainly of red or white fibers. The red *soleus* muscle of the rabbit falls into almost complete tetanus with ten stimuli per second, while the white *gastrocnemius medius* with the same frequency of stimulation gives very evident single contractions. A frequency of six stimuli per second permits the white muscle to relax almost completely

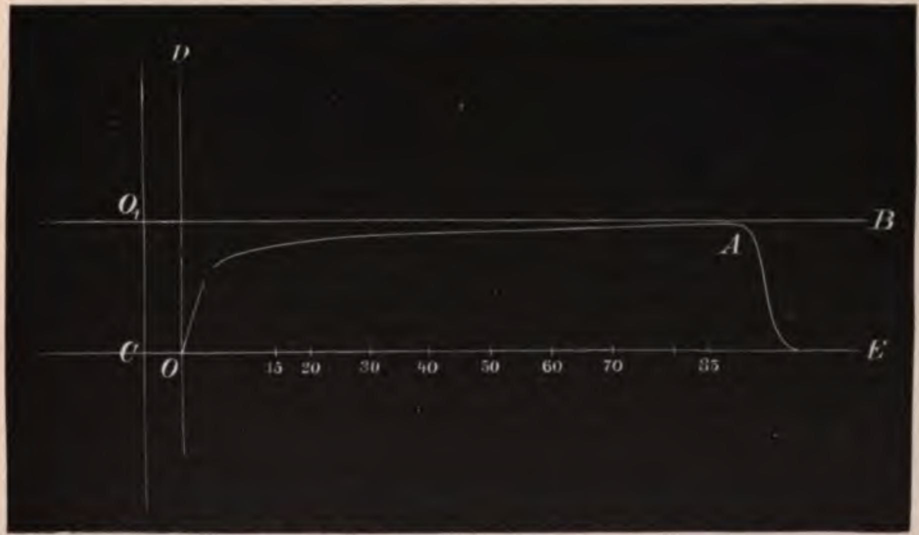

Fig. 166.—Tetanus curve of the frog's gastrocnemius, after Bohr. Twenty-seven stimuli per second.

In practicing any particular movement therefore we are striving to bring about in our central nervous system such a combination of physiological factors as will accomplish the desired effect. The more complicated a movement is, the more difficult it is of course to discover this combination. But after the connection has once been established, the movement can be carried out with the greatest ease in almost a purely mechanical manner.

Here comes in another peculiarity. When we practice a particular movement for the first time, we use a number of muscles which have no importance whatever for the movement intended, but rather interfere with it, since they fatigue the body to no purpose. The further the practice is carried, however, the more we learn to suppress these useless movements; and at the same time the respiration and circulation become more and more exactly adapted to the actual needs. It has been observed that the increase in combustion from a given additional amount of work becomes steadily less (down to a certain limit), as practice continues.

References.—*W. Biedermann*, "Electro-Physiology," translated by Welby, New York and London, 1898.—*R. Du Bois-Reymond*, "Spezielle Muskelphysiologie und Bewegungslehre," Berlin, 1903.—*A. Fick*, "Mechanische Arbeit und Wärmeentwickelung bei der Muskeltätigkeit," Leipzig, 1882.—*A. Mosso*, "Fatigue," English edition by Margaret and W. B. Drummond, New York and London, 1904.

CHAPTER XVI

ON SENSATIONS IN GENERAL

FIRST SECTION

QUALITATIVE RELATIONS BETWEEN STIMULUS AND SENSATION

WE obtain our knowledge of the outside world entirely through our *senses*. The sense of *touch*, taken in its widest acceptation, teaches us to recognize the nature of those objects about us which come into actual contact with our bodies, and gives us information concerning the temperature of these and more distant objects.

By the sense of *taste* we can distinguish certain properties of such substances as can be placed in the mouth.

The sense of *smell* enables us to judge something of the nature of the atmosphere. For certain animals this sense is of very great importance, in that it furnishes the possessor with knowledge of prey or of enemies even at a considerable distance.

By the sense of *hearing* we are made aware of those vibrations of solid, fluid or gaseous bodies, which strike the ear. Through this sense we obtain knowledge not only of what goes on immediately about us, but also of what takes place at a distance.

The sense of *sight* reaches out to a still greater distance. By its help we can penetrate to the farthest point from which light rays can reach the eye.

But our sensations [1] do not all relate to the outside world. From all the organs of the body information of their condition and of the processes taking place within them is all the time being brought by appropriate nerves to the central nervous system. Some of these messages never rise into consciousness, but have a controlling influence on the functions of the body through the lower nerve centers. Others rise to the plane of consciousness and eventuate

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[1] By sensation we mean the simplest possible state of consciousness, one which cannot be analyzed into simpler components. But a sensation corresponding to this definition probably never exists, for psychological analysis has demonstrated that even the simplest conscious processes are really composed of several simple sensations. For example, the simple sensation of sweetness is always associated with the feeling that we have something in the mouth; the sensation of a color likewise is complicated by its projection to a certain place in the outside world, etc. These processes in consciousness we shall designate as ideas.

It will be understood that the terms *weak*, *medium*, and *strong* as applied to the current in this discussion do not designate any absolute values of the current, since what is medium current for one nerve-muscle preparation may be strong for another. The terms are purely relative to any given preparation.

This peculiar behavior of a nerve-muscle preparation to currents of different strength, which finds expression in the law of contraction, depends upon another law enunciated by Pflüger, namely, that a constant current has no stimulating action on the nerve between the poles, but acts only at the poles. *On closing the current the stimulus starts from the cathode, on opening from the anode.*

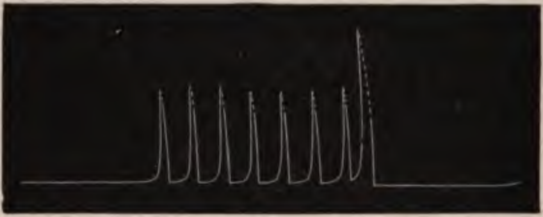

FIG. 161.—Catelectrotonus. The tracing is to be read from right to left. The nerve was first stimulated in the neighborhood of the cathode of the polarizing current with stimuli too weak to produce any effect while the polarizing current was not running. The polarizing current was then turned on, and, without changing the strength of the stimuli, they became effective. When the polarizing current was again turned off, the stimuli were again subminimal.

This *polar law of excitation* may be illustrated by the following experimental facts. If in stimulating with the constant current the electrodes be applied to the nerve as far apart as possible, and the latent period of the closing contractions be determined both for the ascending and descending currents, we find this period to be longer for the former than for the latter (v. Bezold). With the descending current the cathode is nearer the muscle than with the ascending current; hence the stimulus has a shorter distance to travel to reach the muscle with the former than with the latter. In a similar way it can be shown that the stimulus starts from the anode when the current is broken.

The *law of contraction* may be illustrated by carrying the experiment farther. Thus if from the determinations of the latent period just mentioned the rate of transmission of the stimulus be calculated, it will be found considerably lower than when it is determined on the same nerve, by the method (described on page 417) of stimulating at two points with the induction current. The reason is that with the ascending current the stimulus on its way to the muscle has experienced some resistance at the anode. This resistance varies considerably in amount according to the strength of the stimulating current. When the current is weak or of medium strength the stimulus at the cathode on closing the current is strong enough to overcome the resistance at the anode. But when the current is strong the resistance at the anode is too great to be overcome by the stimulus at the cathode, and it constitutes therefore a complete block. It can be shown also that when the cathode intervenes between the anode and the muscle, it creates a resistance to the anodic stimulus.

The polar law of excitation was deduced by Pflüger mainly on the ground of the alterations in excitability produced in the nerve by a constant current.

While the current is flowing the *excitability is increased* on both sides of the cathode; on both sides of the anode it is *decreased*. These alterations appear immediately (within 0.00007 second at most) after closing the current. In the intrapolar region there is found an indifferent point where the excitability of the nerve is not changed; and as the constant current increases in strength this point moves toward the cathode. At the same time the extrapolar alterations of excitability spread over greater lengths of the nerve.

Likewise during the first few moments after the current is opened alterations in the excitability appear, but they are just the reverse of those which occur while the current is closed—i. e., reduced at the cathode and increased at the anode.

These alterations may be studied in the following manner. A nerve is stimulated rhythmically, say once a second, with a current of constant strength, and the resulting contractions are recorded in the usual manner. If now while the stimulation is going on at the regular rhythm, a constant current be led into the nerve, and the stimuli fall in the neighborhood of the cathode of this current, the contractions at once become stronger; if they fall in the neighborhood of the anode, the contractions decrease in size and disappear altogether (see Figs. 161 and 162). When the current being led through the nerve is broken, contractions from stimuli applied at the cathode become smaller, those from stimuli at the anode become larger.

The increase of excitability at the cathode while the current is closed soon fails and passes over into a depressed condition, which, as Biedermann observes, is probably the expression of a local fatigue of the nerve.

The phenomena comprehended under the law of contraction may then be explained through the law of polar excitation as follows: *Weak currents* give a closing contraction because when the current is closed, the sudden rise in irritability of the nerve at the cathode is great enough to constitute a stimulus of itself. The stimulus is effective whether the current be ascending or descending, for in the one case the cathode is toward the muscle, and in the other the resistance at the anode, due to the decrease in irritability, is not great enough to block the stimulus. The sudden increase in excitability produced in the nerve at the anode when the current is broken is not yet sufficient to constitute a stimulus.—With the *medium current* the increase in excitability at the cathode on closing and at the anode on opening are both sufficient to produce a stimulus, and in neither case is the opposite pole strong enough to block it. The *strong current* is distinguished from the medium by the circumstance that while the current is closed the resistance at the anode is stronger than the excitation at the cathode and *vice versa* when the current is opened. Consequently with the ascending current the excitation started at the cathode cannot break through

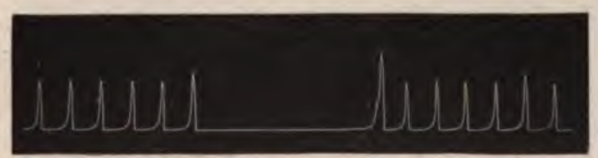

FIG. 162.—Anelectrotonus. The tracing to be read from right to left. A series of stimuli just strong enough to produce slight contractions were applied in the neighborhood of the anode for the polarizing current. When the polarizing current was turned on the stimuli became ineffective. When it was again turned off the stimuli again became effective.

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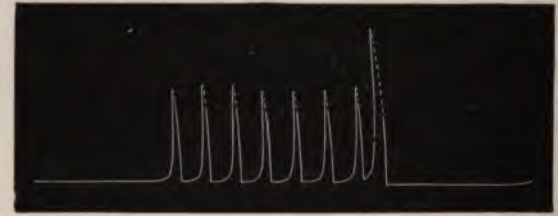

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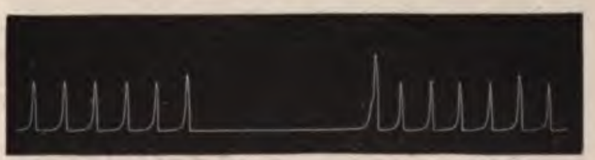

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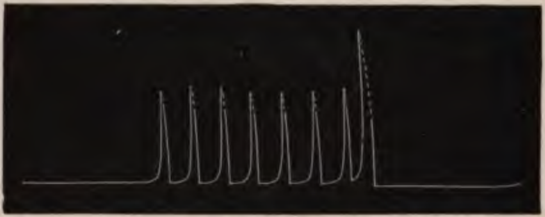

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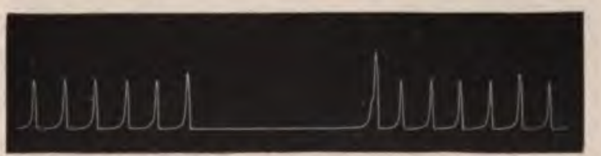

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the anode, and the closing contraction is wanting. With the descending current the excitation started at the anode meets with a resistance at the cathode which may or may not completely block it; hence the opening contraction either fails altogether or is greatly diminished.

Exactly the same laws hold for the *induction currents* as for the constant current. They also stimulate at the cathode as they appear and at the same time produce a resistance at the anode. When they are strong enough, they have a stimulating effect also as they disappear and then the stimulus starts from the anode.

The fact that the induction currents produce a resistance at their anode is demonstrated by the following experiment: a nerve is stimulated with ascending induction currents which, beginning with very weak shocks, are gradually increased in strength (Fig. 163). The height of the contractions at first increases, but after a time decreases, and with a certain strength the muscle remains at rest (Fig. 163; Nos. 11–18). If the strength of the shocks be raised still further, contractions appear again, which at first are weak (Nos. 19, 20), but gradually become stronger until they finally may become supramaximal. With a

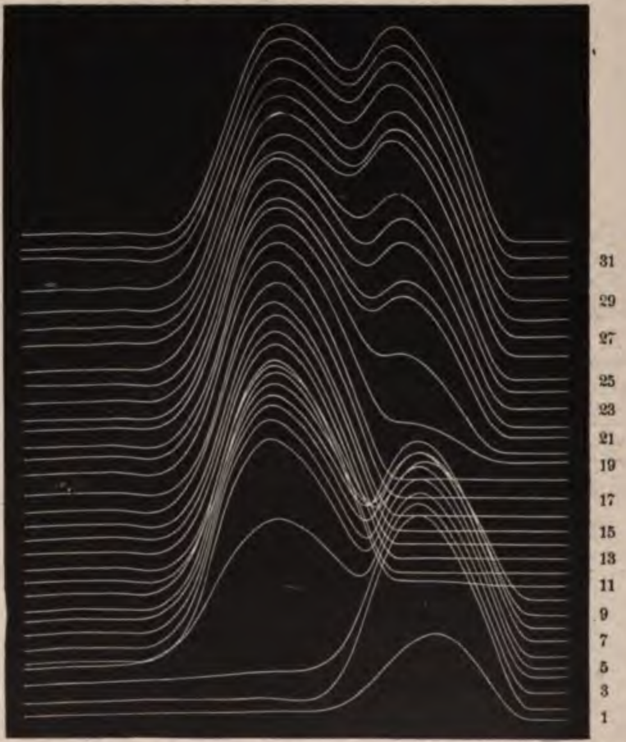

FIG. 163.—Stimulation of a nerve by a series of ascending make- and descending break-induction shocks of increasing strength. To be read from right to left. The first contraction of each pair was obtained by the ascending closing and the second by the descending opening shock. There are no "gaps" in the latter series.

The presence of different temperature points has been established not only by use of the appropriate temperature stimuli but also by mechanical, electrical and chemical stimulation.

The sensation which is produced by stimulation of a single temperature point is not "pointlike"; instead, one experiences a sort of irradiation of the feeling, so that the sensation is more extensive than the temperature point —i. e., it appears to be disklike and at the same time to have depth. It is on this account that the temperature sensations aroused by contact with warm and cold objects appear to be perfectly continuous, giving no indication of the pointlike arrangement of the end organs. Then we are inclined also to fill up unconsciously all the gaps in our special sensations (cf. the blind spot in the eye, Chapter XXI).

The number of cold spots in the skin of an adult is found to be 6–23 per square centimeter of surface; the number of warm spots 0–3. The entire surface of the body would contain, therefore, about 250,000 cold spots, and about 30,000 warm spots. In a child the temperature points appear to stand closer together, and this may be taken to mean that the child is born with his complete equipment of such points.

In order to obtain a more accurate idea of the topography of the temperature senses, Goldscheider has stimulated different portions of the skin with the ends of cold and hot rods 3–4 cm. in diameter. One cannot obtain the number of temperature points by this method, but can test the relative sensitivity of different regions very well. Thus if there be no temperature points in a certain portion, application of the rods will produce no sensation of temperature at all; if points are present, they may vary both in number and excitability, so that the degree of sensitivity will vary. A surface with only a few *intense* points would give a stronger sensation than another with many *weak* points, etc. Fig. 183 is given as an example of the topographical distribution of the cold and heat senses.

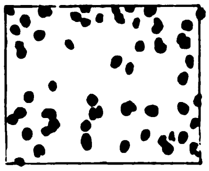

FIG. 182.—The arrangement of cold spots (green), heat spots (red), and pressure spots (black) on a small area of the dorsal side of the left wrist, after Blix.

Goldscheider summarizes his numerous experiments on this subject as follows: (1) The cold sense is everywhere more perfectly developed both extensively and intensively than the heat sense. (2) This relationship holds as well for the parts of the skin habitually clothed as for the parts habitually naked. Goldscheider finds the cause of this regional difference in the varying number of nerve fibers supplied to the different places. Of course there should be added also the varying thickness of the epidermis covering the end organs.

The experiments of different authors agree fairly well with regard to the acuteness of the temperature senses in the different regions. Those most sensitive to temperature stimuli are the nipples, and the breast in general, the alæ nasæ, the anterior parts of the arm; then follow the outer angle of the eye, the upper lip, the abdomen, the volar side of the forearm, the inner parts of the thigh, the foreleg, etc. Least sensitive of all is the scalp.

The hand is but slightly sensitive to temperature and in general it can be said that those regions of the skin which are used especially for touch are less sensitive to temperature than other regions.

of different size, a large one (12 × 6 cm.) applied to the breast, and a small one (0.5–2 cm. diameter) applied over the motor point to be tested. Suppose now the large electrode is the anode: the current enters then with relatively low density, spreads out through the body with still less density and finally collects at the cathode with great density. Since now the effects of a current depend upon its density, it follows that with currents of moderate strength these effects will appear only at the smaller electrode. Some of the many threads of current reaching the smaller electrode from all parts of the body, will necessarily pass through the nerve under it. The effective cathode of the current lies where these threads pass out of the nerve, and if, as we have assumed, the smaller electrode is the cathode, other things being equal, the current will have its greatest possible density there. If the current is reversed so that it now enters the body by the smaller electrode (which is still over the nerve), the places where the threads of current leave the nerve constitute as before the effective cathode; the density of the current now however is less than in the first case (Fig. 165).

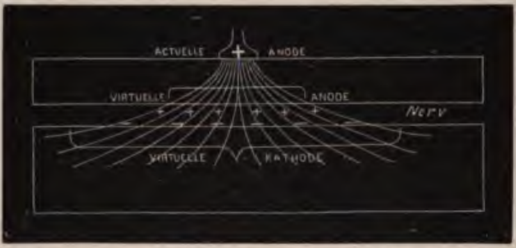

FIG. 165.—Schematic representation of the entrance into and exit from a nerve of a current applied to the skin over the nerve, after de Watteville.

The polar law of excitation applies also to muscle, both with the constant and induction current (v. Bezold, Engelmann, Biedermann; cf. page 416).

We have a very instructive proof of this in the "polar failure" of excitation discovered by Biedermann and Engelmann. If, for example, the end of a frog's sartorius muscle be narcotized and the cathode be applied to this injured place, on closing the current the muscle remains at rest. The normal muscle substance is not stimulated by the closure of a current as it passes from the normal to the paralyzed or dead muscle substance, and the mere passage of a current is not sufficient to discharge the contraction (Locke and Szymanowski). Similar phenomena may be shown on opening of the current when the anode is placed at the injured place.

E. EFFECT OF A RAPID SERIES OF STIMULI

If a nerve or a muscle be affected by two stimuli in rapid succession, so that the action resulting from the first has not yet come to an end when the second becomes effective, the relaxation which would otherwise follow the first contraction is interrupted and the effect of the second stimulus *is added to* the first; consequently the contraction of the muscle is greater than it commonly would be as the result of a single stimulus. It is only when the load of the muscle is very light that it contracts as strongly to a single stimulus as to rapidly repeated stimuli (v. Frey).

In *summated contractions* the ascending limb of the second contraction curve is steeper than that of the first, hence the summit of the second appears earlier than would be expected if its course were the same as the first (v. Kries). The latent period of the superimposed contraction is also said to be very much shorter than that following the first stimulus (Fick).

In order that successive stimuli may produce a summation they must not follow one another too rapidly. The smallest interval possible for any given preparation depends upon the temperature and the strength of the stimuli: for the nerves of the frog at ordinary room temperature it may be estimated at about 0.001 to 0.005 second. We have a *refractory period* therefore in nerves and skeletal muscles just as we have in heart muscle (cf. page 183).

If more than two stimuli affect the nerve or muscle at sufficiently short intervals the contraction of the muscle becomes still greater, and its curve is perfectly continuous, showing no separate summits (cf. Fig. 166). This form of contraction is called *tetanus*.

Complete tetanus appears only when the stimuli follow one another so rapidly that the interval between them is less than the time occupied by the active shortening of the muscle when that is maximal. The frequency depends therefore primarily upon the behavior of the muscle to single stimuli; the more rapidly a single contraction runs its course, the more frequently must the stimuli be given to produce complete tetanus. This is beautifully shown by the behavior of muscles of warm-blooded animals composed mainly of red or white fibers. The red *soleus* muscle of the rabbit falls into almost complete tetanus with ten stimuli per second, while the white *gastrocnemius medius* with the same frequency of stimulation gives very evident single contractions. A frequency of six stimuli per second permits the white muscle to relax almost completely

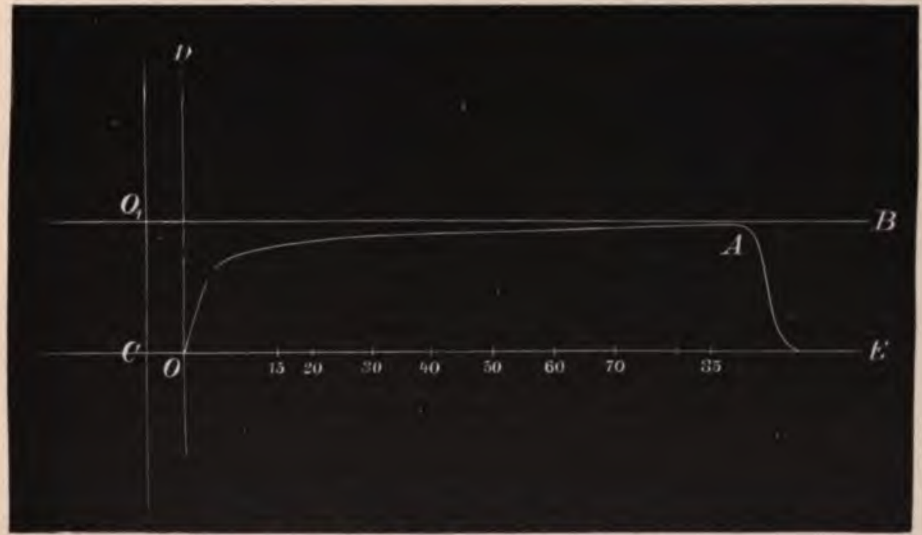

FIG. 166.—Tetanus curve of the frog's gastrocnemius, after Bohr. Twenty-seven stimuli per second.

between contractions, whereas it keeps the red muscle almost continuously contracted (Ranvier, Kronecker and Stirling; cf. Fig. 167).

Everything which tends to make the single contractions occupy more time operates to reduce the frequency of stimulation necessary to evoke complete tetanus. Thus fatigued muscles are thrown into tetanus with a lower frequency than unfatigued, because their contractions are slower.

The more the frequency is reduced below that which is just sufficient to produce tetanus, the more distinctly do the contractions produced by the individual stimuli stand out from one another, until finally below a certain frequency there is no fusion whatever. We have therefore all possible gradations between the isolated contractions and complete tetanus. This suggests that tetanus itself, notwithstanding the continuous curve by which it is represented graphically, is really a discontinuous process, and complete proof of this is furnished by the electrical variations accompanying tetanus (page 433).

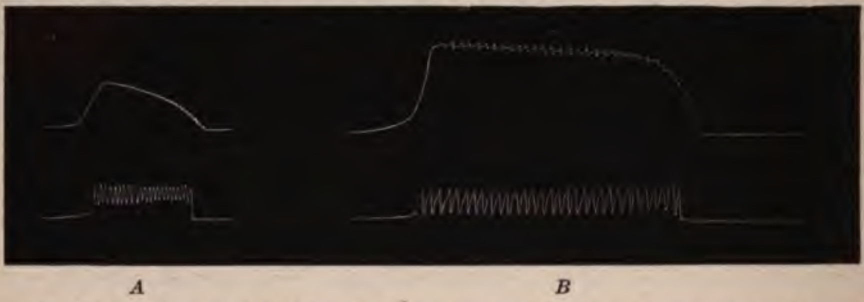

FIG. 167.—Tetanus curves of the white (lower tracings) and of the red (upper tracings) muscles of the rabbit, after Kronecker and Stirling. To be read from right to left. *A*, ten stimuli per second. *B*, six stimuli per second.

How are we to conceive of the processes going on in the muscle in tetanus? One significant fact is that by artificially supporting the muscle, so that it does not lift its weight until it has contracted some distance, the single contractions can be made to reach the same height as tetanus with the same strength of current (v. Frey). We may say, therefore, that in tetanus the muscle contracts to its utmost, because to a certain extent it is supported on itself. In addition to this the *irritability* of both nerve and muscle is increased by a previous stimulation—i. e., if the excitation is not too strong or does not continue so long as to involve much fatigue. Hence not infrequently it happens that stimuli, which of themselves are ineffective, become effective merely by being repeated with sufficient frequency.

Tetanus may be looked upon therefore as a sort of *heaping up* of small contractions due to the rapidity of the stimuli and to increased irritability.

F. VOLUNTARY CONTRACTIONS

If we compare voluntary contractions on the same drum with the rapid, twitchlike muscular contraction produced by a single artificial stimulus, we discover that the former are both *slower and less abrupt.* Comparing them with the contractions obtained by rapidly repeated shocks, we find more in common. Many other circumstances strongly support this resemblance, the most important of them being, that the voluntary contraction as well as the contractions which appear reflexly with strychnine poisoning are accompanied,

just as tetanus is, by action currents which signify a discontinuous excitation (Lovén). But it is worthy of note that the rhythm of these action currents in voluntary contractions, and others produced under the influence of the central nervous system, is only about half as rapid as the frequency of stimulation necessary to produce a complete tetanus. And yet the voluntary contraction as ordinarily recorded is quite continuous. This must be due to the fact that the single impulses sent out to the muscles from the central organs to produce a voluntary contraction last longer than the ordinary instantaneous stimuli (Lovén), and that the separate twitches are therefore more readily fused. We know, indeed, that a "time stimulus" (page 423) is longer drawn out than a momentary stimulus and that it is therefore better adapted to produce summation with a low frequency of stimulation.

The trembling of the muscles which accompanies a strained effort to overcome some great resistance or an attempt to hold a muscle contracted voluntarily to its utmost, are generally regarded as expressions of the individual impulses discharged from the central nervous system. The regulation of the innervating mechanisms would seem in these cases to be disturbed in some way so as to affect the fusion of the separate contractions. It has been shown that the number of such oscillations per second varies in man from seven or eight to twelve or thirteen (Lovén, v. Kries, Schäfer). The greatest muscular efforts are made, it appears, with a frequency of ten to twelve impulses per second.

§ 4. SIGNS OF ACTIVITY IN MUSCLE AND NERVE

A. ELECTRICAL PHENOMENA

1. *Action Current.*—The general law of the electrical variation known as the action current, which makes its appearance when nerve or muscle is active, has already been given on page 48. In view of its great importance for the general physiology of muscles and nerves, however, we must discuss it here somewhat more in detail.

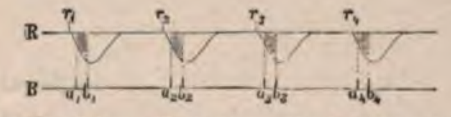

FIG. 168.—Schema illustrating a rheotome experiment.

In order to study time relations of the action current, one can use either the capillary electrometer whose excursions can be recorded by the photographic method, or the repeating rheotome of Bernstein.

Suppose we have an electrical variation of the form represented in Fig. 168. The galvanometer is too slow to reproduce this form correctly. But if we arrange the experiment so that a definite portion of each variation of the current—e. g., that included between a_1 and b_1 in Fig. 168—affects the galvanometer, and this is repeated many times, from the excursion of the galvanometer we can learn the extent of the electrical variation during this portion. If now we can determine in the same way the excursion of the galvanometer for the other

portions, say b_1 to c_1, c_1 to d_1, d_1 to e_1, etc., of course it will be possible to obtain the form of the entire variation. An apparatus which would enable us to make such determinations must permit of connection with the galvanometer at a definite moment after the beginning of the variation, and of breaking this connection at any desired moment during the variation. Since the electrical variation in muscles and nerves is started by the excitation, the requirements will be met if the galvanometer circuit can be closed or broken at any given interval after the instant of stimulation.

The *rheotome* of Bernstein (Fig. 169) consists of a wheel (r) revolving about a vertical axis, and carrying on its circumference three metal pegs, one of which (c) gives the stimulus to the nerve by closing or opening the primary current to an induction coil; the other two pegs insulated from the first, but in electrical connection with each other, serve to close and open the galvanometer circuit. At each revolution of the wheel the pegs c_1 and c_2 dip into the mercury troughs (q_1 and q_2) respectively which are connected with the muscle on the one hand and the galvanometer on the other. The mercury troughs are movable with respect to each other, so that the duration of the galvanometer current can be varied within wide limits. If now the wheel is revolved at a certain speed, with each revolution the muscle will receive a stimulus and the galvanometer circuit will be closed for a certain definite time after each stimulus. If we have the two contacts so arranged that the galvanometer is connected with the muscle at the same instant that the stimulus is given, the excursion of the galvanometer will represent the first part of the variation evoked by the stimulus. Then by shifting the contacts, the galvanometer can be connected at different intervals following the instant of stimulation until the entire variation is recorded.

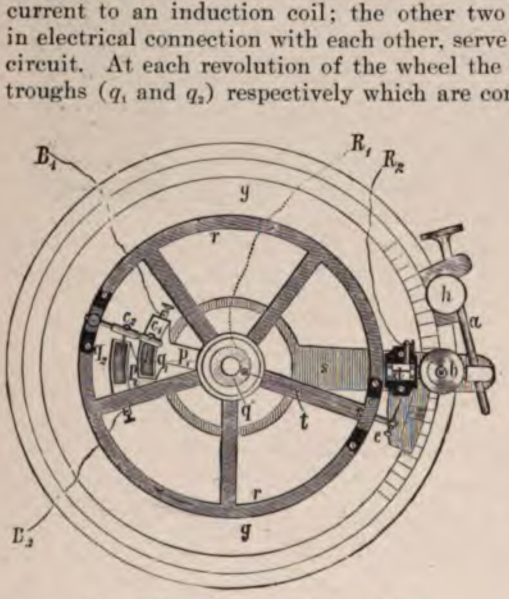

Fig. 169.—Rheotome of Bernstein.

If a muscle (or the heart) or a nerve be connected at two uninjured places (a and b, Fig. 170) with a galvanometer, and it be then stimulated at some outside point (c), the galvanometer shows that the point a situated nearer the point of stimulation becomes electrically negative to b, and then the current is reversed and b becomes negative to a (cf. pages 48 and 179). The *action current therefore consists of two phases*, each of which gives expression to the general law, that every active point of a muscle or nerve is electrically negative to every resting point (page 48). When the excitation spreads from the point c, the nearer of the two points naturally becomes active first, while the more distant point (b) is still resting; hence the first phase. When the excitation reaches the point b and the point a first stimulated has gradually passed into a resting state, the second phase appears.

The action current does not represent an artificial product, but is a process intimately connected with the process of excitation, for it is produced by all kinds of stimuli; it is propagated at the same rate of speed as the excitation and varies in strength to a certain extent with the strength of stimulation.

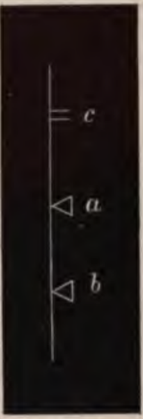

Fig. 170.—Schema illustrating spread of an excitation causing an action current.

If the nerve or the muscle be led off to the galvanometer, not from two points on the longitudinal surface, but from the longitudinal surface and a cross section, the second phase of the action current no longer appears, but the current is now directed from the longitudinal surface over to the cross section. It was in this form that the action current was first discovered. Since it runs in the opposite direction from the current of rest (see page 48) it was designated by Du Bois-Reymond as the *negative variation* of the current of rest.

The action current is the only functional change which we have thus far been able to observe in living nerves. It is of great importance also for the reason that it permits us to determine the *nature of any muscular contraction.*

We have already become acquainted with an example of this in studying the heart. The action current there showed us that, notwithstanding its long duration, the contraction of the heart is in reality a simple muscular twitch (cf. page 179).

There are other kinds of contractions, like tetanus and voluntary contractions, which as we have seen are apparently continuous, but which the action current proves to be discontinuous. If by the use of the rheotome, a muscle be stimulated often enough to produce complete tetanus, the excursions of the galvanometer will show that each separate stimulus produces a special action current of its own—i. e., every excitation causes a molecular change in the muscle, although the change may not be apparent in the mechanical behavior of the muscle.

The action current of muscle as well as of nerve is strong enough to have a stimulating action of its own (Matteucci). If the nerve of one muscle, B, be laid across the belly of another muscle, A, and the second muscle be then stimulated through its own nerve, with each contraction of A, B also contracts, and this even in case A is so tense that it no longer changes its form. The contractions of B agree minutely in number, strength and sequence with those of A. If A is tetanized, B also is tetanized. These phenomena are called *secondary contractions*, secondary tetanus, etc.

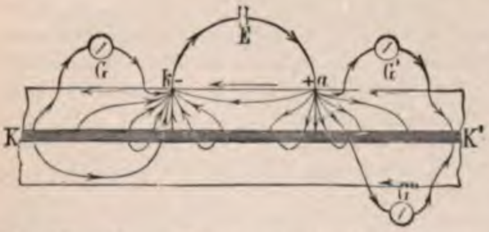

Fig. 171.—Illustrating the theory of electrotonic currents, after Hermann.

2. *Electrotonic Currents.*—When an electric current is conducted through a certain length of a medullated nerve and another portion of the nerve outside of this length is connected with the galvanometer, an

tion to them they gradually become more and more unpleasant and, finally, actually painful.

In diseases accompanied by pain, the pain is often more severe at night than during the day. This is probably due to the fact that in the daytime our attention is distracted by many things outside ourselves, and is not directed so exclusively to the body.

By purposely fixing one's attention on a definite object or idea it is possible to suppress not only the expression of pain, but to a large extent the pain itself. The following story of Immanuel Kant is much to the point. Kant suffered from time to time with attacks of gout which, as many know, may be very painful. "Out of patience at feeling myself deprived of sleep," he writes, "I soon seized upon the stoical expedient of fixing my thought intently on some chance object, whatever it might be (e. g., on the many ideas associated with the name of Cicero), and of consequently diverting my attention from all sensations. In this way the sensation speedily became blunted, so that the natural tendency to sleep overcame them. And this I could repeat with equally good results each time in the little interruptions in my night's rest occasioned by recurring attacks. But in the morning the shiny redness of the toes of my left foot was sufficiently convincing to myself that these sensations had not been purely fanciful."

Although all men have not the same will power as Kant had, we may nevertheless learn from his example that it is possible actually to suppress pain to a certain extent, just as it is possible for us to accustom ourselves to bear a necessary pain without sounding it abroad with loud wailings.

The expression of pain, therefore, is not to be accepted as a measure of its intensity. A strong-willed person may feel very severe pain without wincing, while another may cry out at a pin prick. On the other hand, we must not forget the experience oft confirmed in animals as well as in men that sensitiveness to pain is very different in different individuals. And since nobody can tell with certainty how strong is the pain which another feels, we ought not to withhold our sympathy from others when they give expression to pain.

It is very difficult to decide just wherein lies the *real physiological cause of pain.* Since we know that the pain aroused by any adequate stimulus has an altogether different character in different parts of the body—as, e. g., those aroused by a high temperature differ from those aroused by a low temperature, as the pain of muscle cramps is of a different kind from that of high pressure inside the eye, and the pains occurring in inflammatory processes differ according to the organ inflamed—the assumption is undoubtedly suggested that pain is produced by an excessive excitation of the ordinary afferent nerves from different parts of the body.

The fact that in certain diseases of the nervous system the sensations of pain are lost while the ordinary tactile sensations do not suffer any considerable diminution, does not militate against this hypothesis. One might readily imagine that the maximum excitation necessary for the production of pain were not reached, although the threshold stimulus remained approximately the same; and this supposition could be brought into line with Schiff's observation that section of the gray matter of the spinal cord abolishes sensations of pain without affecting the tactile sensations.

Proceeding from this observation it has repeatedly been conjectured that painful impressions are conducted through the gray matter, and that the

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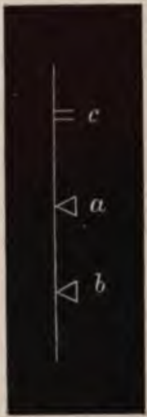

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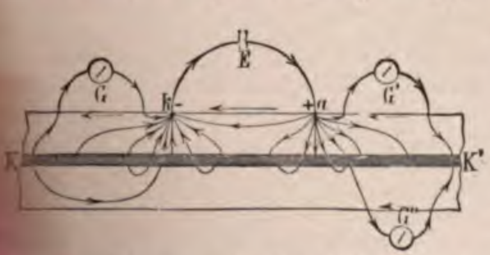

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rough a certain length of a medullated nerve and another portion rve outside of this length is connected with the galvanometer, an sation of pressure accompanying the stimulus fails, while the painful after-effect appears very vividly.

With regard to the topographical distribution of the pain spots we learn from v. Frey and others that on the back of the hand over the metacarpus of the ring finger 16 pain points, as against 2 pressure points, can be demonstrated within 12.5 sq. mm.—i. e., 1.3 pain points to the square millimeter.

From reasoning which we need not enter into here v. Frey has reached the following conclusions with regard to the anatomical structures which may possibly serve as the end organs of the different cutaneous nerves:

(1) Among the well-known sensory nerve endings on parts devoid of hair there is only one form which occurs in sufficient number to fulfill the requirements of an end organ of the pressure points, namely, the *tactile corpuscles* of Meissner. According to this discoverer there are—e. g., over the metacarpus of the little finger in 1 sq. mm. one to two of these corpuscles—which agrees well with the number of pressure points in the same place.

(2) These corpuscles however are quite exclusively confined to the parts devoid of hair. Anatomical investigations have brought to light the presence of a *wreath of nerve fibers* encircling the hair follicles down close under the opening of the sebaceous glands, their terminal processes penetrating the walls of the follicle as far as the glassy layer. This wreath of nerve fibers which occurs with the greatest regularity in every hair follicle may be the end organ of the pressure points associated with the hairs.

(3) The sensation of pain is probably aroused by stimulation of some mechanism lying nearer the surface. Since only free intraepithelial nerve endings are found external to the tactile corpuscles, we may look upon these as the organs of the (superficial) sensations of pain in the skin.

(4) Finally, v. Frey and Thunberg, the latter by careful analysis of the different phenomena attending stimulation with heat, have made it probable that the end organs of the heat nerves lie deeper than those of the cold nerves, also that the latter lie deeper than the end organs of the pain nerves.

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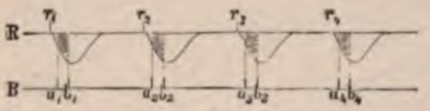

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the anode, and the closing contraction is wanting. With the descending current the excitation started at the anode meets with a resistance at the cathode which may or may not completely block it; hence the opening contraction either fails altogether or is greatly diminished.

Exactly the same laws hold for the *induction currents* as for the constant current. They also stimulate at the cathode as they appear and at the same time produce a resistance at the anode. When they are strong enough, they have a stimulating effect also as they disappear and then the stimulus starts from the anode.

The fact that the induction currents produce a resistance at their anode is demonstrated by the following experiment: a nerve is stimulated with ascending induction currents which, beginning with very weak shocks, are gradually increased in strength (Fig. 163). The height of the contractions at first increases, but after a time decreases, and with a certain strength the muscle remains at rest (Fig. 163; Nos. 11–18). If the strength of the shocks be raised still further, contractions appear again, which at first are weak (Nos. 19, 20), but grad ally become stronger until they finally may become supramaximal. Wit

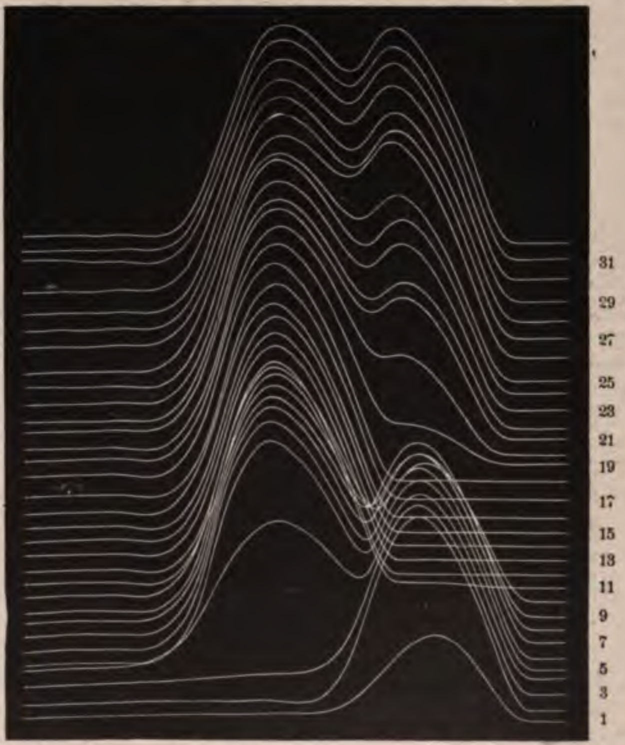

FIG. 163.—Stimulation of a nerve by a series of ascending make- and descending break-induction shocks of increasing strength. To be read from right to left. The first contraction of each pair was obtained by the ascending closing and the second by the descending opening shock. There are no "gaps" in the latter series.

Likewise the thyroarytenoid muscle, whose finely graduated contractions determine the pitch of the vocal tones, appears to possess a very delicate muscular feeling produced by the afferent nerves; there is, however, no feeling of movement connected with this.

According to the view which Goldscheider in particular has worked out, the most important nerves for the perception of passive movements are the *afferent nerves of the joints.* The sensations of pressure and tension in the soft parts of the limbs not only do not produce the sensation of movement, they even interfere with it. Again, since the threshold value of the sensation —i. e., the smallest passive movement which one can perceive—is not influenced in any way by the degree of contraction of the muscles when the passive movement begins, coöperation of the muscular sensibility as a factor appears to be excluded. Finally the distance described by the moving force bears no relation to the amount of sensation which one experiences; the determining factor is the amount of rotation at the joint.

Lewinski made some experiments on ataxic patients (cf. page 472) by moving their limbs very slowly and very slightly at the ankle, knee and hip joints, part of the time pressing the parts together at the joint, part of the time not. When the parts were thus pressed the patients always perceived the movement very exactly, when not they could form no idea of the motion.

The *perception of active movements* likewise results from the rotation of the joints. To this are to be added, however, as contributing factors the sensations connected with the tension of the tendons and their epiphyses, possibly also the sensations aroused through the sensory nerves of the muscles. These sensations concern not merely the tendons, etc., of the active muscles, but also their antagonists. In a passive movement the tendons simply follow the pull; some are stretched, others are only under the tonic resistance of their own muscles.

In active movements, especially if the joint to be moved is loaded, we also experience sensations of *weight* and of *resistance.* The nerves of the joints and of the tendons are again of the first importance, the pressure on the surface of the joints and the tension of the tendons varying according to the resistance or the weight.

Jacobi has called attention to still another circumstance to which he ascribes great importance in the determination of the size of a weight, namely, the comparison of the amount of nerve force employed with the latent period of the movement—i. e., the time which elapses between the act of volition and the inception of the movement. The latent period, in his opinion, depends upon the amount of nerve force employed, and with the same amount of nerve force is proportional to the size of the weight.

The *sensory nerves of the skin* appear commonly to be of but slight importance in any kind of motor sensations. The sensation of weight remains unchanged after the skin is rendered insensitive to touch. And yet cutaneous sensations appear to contribute something to the quantitative refinement of a sensation of resistance as well as to the localization of the sensation and so to the formation of a clearer total impression (Goldscheider and Blecher).

the anode, and the closing contraction is wanting. With the descending current the excitation started at the anode meets with a resistance at the cathode which may or may not completely block it; hence the opening contraction either fails altogether or is greatly diminished.

Exactly the same laws hold for the *induction currents* as for the constant current. They also stimulate at the cathode as they appear and at the same time produce a resistance at the anode. When they are strong enough, they have a stimulating effect also as they disappear and then the stimulus starts from the anode.

The fact that the induction currents produce a resistance at their anode is demonstrated by the following experiment: a nerve is stimulated with ascending induction currents which, beginning with very weak shocks, are gradually increased in strength (Fig. 163). The height of the contractions at first increases, but after a time decreases, and with a certain strength the muscle remains at rest (Fig. 163; Nos. 11–18). If the strength of the shocks be raised still further, contractions appear again, which at first are weak (Nos. 19, 20), but gradually become stronger until they finally may become supramaximal. With a

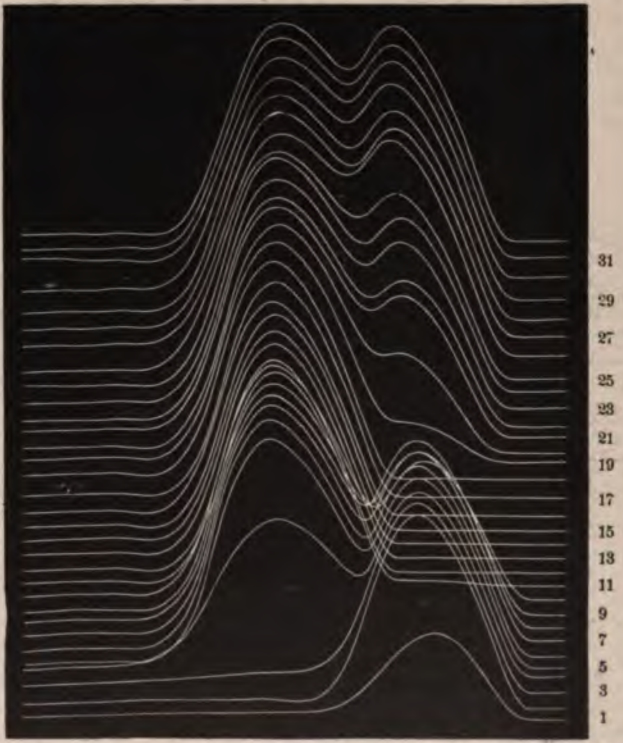

Fig. 163.—Stimulation of a nerve by a series of ascending make- and descending break-induction shocks of increasing strength. To be read from right to left. The first contraction of each pair was obtained by the ascending closing and the second by the descending opening shock. There are no "gaps" in the latter series.

series of shocks of increasing strength we have therefore a gap in the resulting contractions (Fick). This is only observed with the ascending currents, and is the result of a block at the anode. The absence of the contractions is therefore entirely analogous to the corresponding phenomena for the strong ascending constant current. The contractions coming after the gap and gradually increasing in size are produced really by the excitation taking place at the disappearance of the induction current, and are to be regarded for this reason as a sort of opening contractions. But further discussion of their nature here would carry us too far afield.

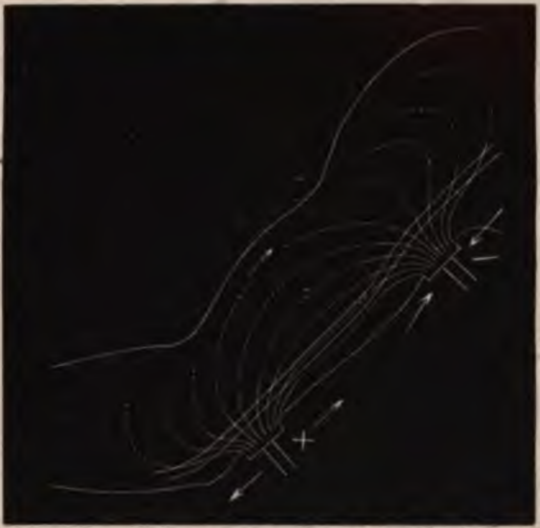

Fig. 164.—Schematic representation of the distribution of an electric current in a human arm on application of two electrodes over a nerve, after de Watteville.

The stimulating effects and the alterations of excitability produced by the electric current follow the same laws in human nerves as in the exsected frog's nerves (Waller and de Watteville).

In experiments on living men, the electrodes of course cannot be applied to the nerves themselves, but can only be placed on the skin; the nerve is stimulated then only by the threads of current which penetrate that far. It will be clear at once that the density of that portion of the current reaching a particular nerve will be greater the nearer the nerve lies to the surface of the skin. Consequently in using the current for therapeutic purposes the electrodes are applied to the skin at those points where the nerve, which it is desired to stimulate, can be reached most directly.

The effective anode is of course the place where the current enters the nerve itself, the effective cathode, the place where it leaves the nerve. If both poles were to be placed on the skin over the nerve, as in Fig. 164, anodes and cathodes would be present at almost every possible point along the nerve, as indicated by the radiating lines. Evidently such an experiment would not be adapted to the study of electrical effects on human nerves. The monopolar method is therefore used, the current being conveyed to and away from the body by electrodes

of different size, a large one (12 × 6 cm.) applied to the breast, and a small one (0.5–2 cm. diameter) applied over the motor point to be tested. Suppose now the large electrode is the anode: the current enters then with relatively low density, spreads out through the body with still less density and finally collects at the cathode with great density. Since now the effects of a current depend upon its density, it follows that with currents of moderate strength these effects will appear only at the smaller electrode. Some of the many threads of current reaching the smaller electrode from all parts of the body, will necessarily pass through the nerve under it. The effective cathode of the current lies where these threads pass out of the nerve, and if, as we have assumed, the smaller electrode is the cathode, other things being equal, the current will have its greatest possible density there. If the current is reversed so that it now enters the body by the smaller electrode (which is still over the nerve), the places where the threads of current leave the nerve constitute as before the effective cathode; the density of the current now however is less than in the first case (Fig. 165).

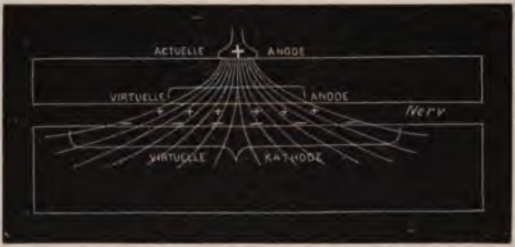

FIG. 165.—Schematic representation of the entrance into and exit from a nerve of a current applied to the skin over the nerve, after de Watteville.

The polar law of excitation applies also to muscle, both with the constant and induction current (v. Bezold, Engelmann, Biedermann; cf. page 416).

We have a very instructive proof of this in the "polar failure" of excitation discovered by Biedermann and Engelmann. If, for example, the end of a frog's sartorius muscle be narcotized and the cathode be applied to this injured place, on closing the current the muscle remains at rest. The normal muscle substance is not stimulated by the closure of a current as it passes from the normal to the paralyzed or dead muscle substance, and the mere passage of a current is not sufficient to discharge the contraction (Locke and Szymanowski). Similar phenomena may be shown on opening of the current when the anode is placed at the injured place.

E. EFFECT OF A RAPID SERIES OF STIMULI

If a nerve or a muscle be affected by two stimuli in rapid succession, so that the action resulting from the first has not yet come to an end when the second becomes effective, the relaxation which would otherwise follow the first contraction is interrupted and the effect of the second stimulus *is added to* the first; consequently the contraction of the muscle is greater than it commonly would be as the result of a single stimulus. It is only when the load of the muscle is very light that it contracts as strongly to a single stimulus as to rapidly repeated stimuli (v. Frey).

In *summated contractions* the ascending limb of the second contraction curve is steeper than that of the first, hence the summit of the second appears earlier than would be expected if its course were the same as the first (v. Kries). The latent period of the superimposed contraction is also said to be very much shorter than that following the first stimulus (Fick).

In order that successive stimuli may produce a summation they must not follow one another too rapidly. The smallest interval possible for any given preparation depends upon the temperature and the strength of the stimuli: for the nerves of the frog at ordinary room temperature it may be estimated at about 0.001 to 0.005 second. We have a *refractory period* therefore in nerves and skeletal muscles just as we have in heart muscle (cf. page 183).

If more than two stimuli affect the nerve or muscle at sufficiently short intervals the contraction of the muscle becomes still greater, and its curve is perfectly continuous, showing no separate summits (cf. Fig. 166). This form of contraction is called *tetanus*.

Complete tetanus appears only when the stimuli follow one another so rapidly that the interval between them is less than the time occupied by the active shortening of the muscle when that is maximal. The frequency depends therefore primarily upon the behavior of the muscle to single stimuli; the more rapidly a single contraction runs its course, the more frequently must the stimuli be given to produce complete tetanus. This is beautifully shown by the behavior of muscles of warm-blooded animals composed mainly of red or white fibers. The red *soleus* muscle of the rabbit falls into almost complete tetanus with ten stimuli per second, while the white *gastrocnemius medius* with the same frequency of stimulation gives very evident single contractions. A frequency of six stimuli per second permits the white muscle to relax almost completely

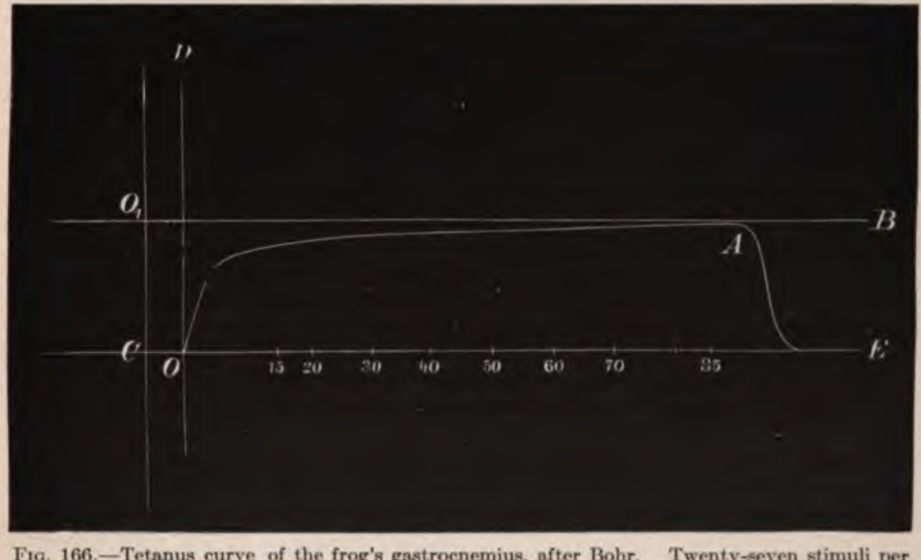

FIG. 166.—Tetanus curve of the frog's gastrocnemius, after Bohr. Twenty-seven stimuli per second.

between contractions, whereas it keeps the red muscle almost continuously contracted (Ranvier, Kronecker and Stirling; cf. Fig. 167).

Everything which tends to make the single contractions occupy more time operates to reduce the frequency of stimulation necessary to evoke complete tetanus. Thus fatigued muscles are thrown into tetanus with a lower frequency than unfatigued, because their contractions are slower.

The more the frequency is reduced below that which is just sufficient to produce tetanus, the more distinctly do the contractions produced by the individual stimuli stand out from one another, until finally below a certain frequency there is no fusion whatever. We have therefore all possible gradations between the isolated contractions and complete tetanus. This suggests that tetanus itself, notwithstanding the continuous curve by which it is represented graphically, is really a discontinuous process, and complete proof of this is furnished by the electrical variations accompanying tetanus (page 433).

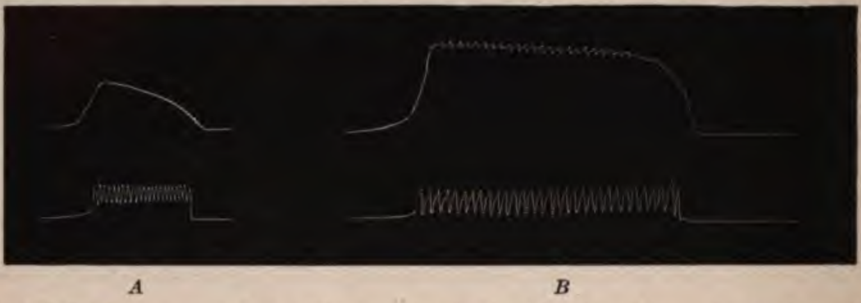

FIG. 167.—Tetanus curves of the white (lower tracings) and of the red (upper tracings) muscles of the rabbit, after Kronecker and Stirling. To be read from right to left. *A*, ten stimuli per second. *B*, six stimuli per second.

How are we to conceive of the processes going on in the muscle in tetanus? One significant fact is that by artificially supporting the muscle, so that it does not lift its weight until it has contracted some distance, the single contractions can be made to reach the same height as tetanus with the same strength of current (v. Frey). We may say, therefore, that in tetanus the muscle contracts to its utmost, because to a certain extent it is supported on itself. In addition to this the *irritability* of both nerve and muscle is increased by a previous stimulation—i. e., if the excitation is not too strong or does not continue so long as to involve much fatigue. Hence not infrequently it happens that stimuli, which of themselves are ineffective, become effective merely by being repeated with sufficient frequency.

Tetanus may be looked upon therefore as a sort of *heaping up* of small contractions due to the rapidity of the stimuli and to increased irritability.

F. VOLUNTARY CONTRACTIONS

If we compare voluntary contractions on the same drum with the rapid, twitchlike muscular contraction produced by a single artificial stimulus, we discover that the former are both *slower and less abrupt.* Comparing them with the contractions obtained by rapidly repeated shocks, we find more in common. Many other circumstances strongly support this resemblance, the most important of them being, that the voluntary contraction as well as the contractions which appear reflexly with strychnine poisoning are accompanied,

just as tetanus is, by action currents which signify a discontinuous excitation (Lovén). But it is worthy of note that the rhythm of these action currents in voluntary contractions, and others produced under the influence of the central nervous system, is only about half as rapid as the frequency of stimulation necessary to produce a complete tetanus. And yet the voluntary contraction as ordinarily recorded is quite continuous. This must be due to the fact that the single impulses sent out to the muscles from the central organs to produce a voluntary contraction last longer than the ordinary instantaneous stimuli (Lovén), and that the separate twitches are therefore more readily fused. We know, indeed, that a "time stimulus" (page 423) is longer drawn out than a momentary stimulus and that it is therefore better adapted to produce summation with a low frequency of stimulation.

The trembling of the muscles which accompanies a strained effort to overcome some great resistance or an attempt to hold a muscle contracted voluntarily to its utmost, are generally regarded as expressions of the individual impulses discharged from the central nervous system. The regulation of the innervating mechanisms would seem in these cases to be disturbed in some way so as to affect the fusion of the separate contractions. It has been shown that the number of such oscillations per second varies in man from seven or eight to twelve or thirteen (Lovén, v. Kries, Schäfer). The greatest muscular efforts are made, it appears, with a frequency of ten to twelve impulses per second.

§ 4. SIGNS OF ACTIVITY IN MUSCLE AND NERVE

A. ELECTRICAL PHENOMENA

1. *Action Current.*—The general law of the electrical variation known as the action current, which makes its appearance when nerve or muscle is active, has already been given on page 48. In view of its great importance for the general physiology of muscles and nerves, however, we must discuss it here somewhat more in detail.

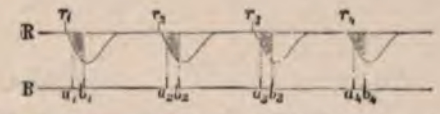

FIG. 168.—Schema illustrating a rheotome experiment.

In order to study time relations of the action current, one can use either the capillary electrometer whose excursions can be recorded by the photographic method, or the repeating rheotome of Bernstein.

Suppose we have an electrical variation of the form represented in Fig. 168. The galvanometer is too slow to reproduce this form correctly. But if we arrange the experiment so that a definite portion of each variation of the current—e. g., that included between a_1 and b_1 in Fig. 168—affects the galvanometer, and this is repeated many times, from the excursion of the galvanometer we can learn the extent of the electrical variation during this portion. If now we can determine in the same way the excursion of the galvanometer for the other

portions, say b_1 to c_1, c_1 to d_1, d_1 to e_1, etc., of course it will be possible to obtain the form of the entire variation. An apparatus which would enable us to make such determinations must permit of connection with the galvanometer at a definite moment after the beginning of the variation, and of breaking this connection at any desired moment during the variation. Since the electrical variation in muscles and nerves is started by the excitation, the requirements will be met if the galvanometer circuit can be closed or broken at any given interval after the instant of stimulation.

The *rheotome* of Bernstein (Fig. 169) consists of a wheel (r) revolving about a vertical axis, and carrying on its circumference three metal pegs, one of which (c) gives the stimulus to the nerve by closing or opening the primary current to an induction coil; the other two pegs insulated from the first, but in electrical connection with each other, serve to close and open the galvanometer circuit. At each revolution of the wheel the pegs c_1 and c_2 dip into the mercury troughs (q_1 and q_2) respectively which are connected with the muscle on the one hand and the galvanometer on the other. The mercury troughs are movable with respect to each other, so that the duration of the galvanometer current can be varied within wide limits. If now the wheel is revolved at a certain speed, with each revolution the muscle will receive a stimulus and the galvanometer circuit will be closed for a certain definite time after each stimulus. If we have the two contacts so arranged that the galvanometer is connected with the muscle at the same instant that the stimulus is given, the excursion of the galvanometer will represent the first part of the variation evoked by the stimulus. Then by shifting the contacts, the galvanometer can be connected at different intervals following the instant of stimulation until the entire variation is recorded.

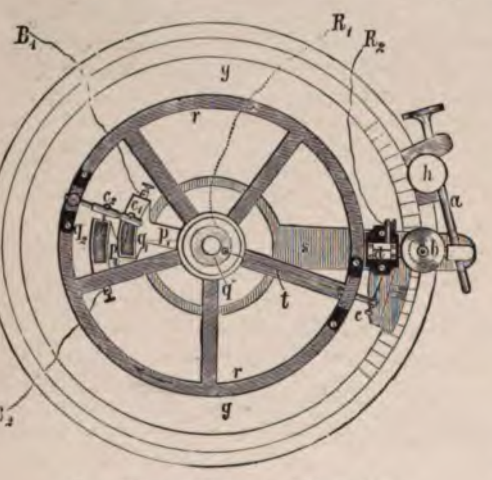

FIG. 169.—Rheotome of Bernstein.

If a muscle (or the heart) or a nerve be connected at two uninjured places (a and b, Fig. 170) with a galvanometer, and it be then stimulated at some outside point (c), the galvanometer shows that the point a situated nearer the point of stimulation becomes electrically negative to b, and then the current is reversed and b becomes negative to a (cf. pages 48 and 179). The *action current therefore consists of two phases*, each of which gives expression to the general law, that every active point of a muscle or nerve is electrically negative to every resting point (page 48). When the excitation spreads from the point c, the nearer of the two points naturally becomes active first, while the more distant point (b) is still resting; hence the first phase. When the excitation reaches the point b and the point a first stimulated has gradually passed into a resting state, the second phase appears.

The action current does not represent an artificial product, but is a process intimately connected with the process of excitation, for it is produced by all kinds of stimuli; it is propagated at the same rate of speed as the excitation and varies in strength to a certain extent with the strength of stimulation.

If the nerve or the muscle be led off to the galvanometer, not from two points on the longitudinal surface, but from the longitudinal surface and a cross section, the second phase of the action current no longer appears, but the current is now directed from the longitudinal surface over to the cross section. It was in this form that the action current was first discovered. Since it runs in the opposite direction from the current of rest (see page 48) it was designated by Du Bois-Reymond as the *negative variation* of the current of rest.

The action current is the only functional change which we have thus far been able to observe in living nerves. It is of great importance also for the reason that it permits us to determine the *nature of any muscular contraction.*

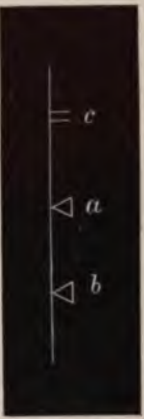

FIG. 170.—Schema illustrating spread of an excitation causing an action current.

We have already become acquainted with an example of this in studying the heart. The action current there showed us that, notwithstanding its long duration, the contraction of the heart is in reality a simple muscular twitch (cf. page 179).

There are other kinds of contractions, like tetanus and voluntary contractions, which as we have seen are apparently continuous, but which the action current proves to be discontinuous. If by the use of the rheotome, a muscle be stimulated often enough to produce complete tetanus, the excursions of the galvanometer will show that each separate stimulus produces a special action current of its own—i. e., every excitation causes a molecular change in the muscle, although the change may not be apparent in the mechanical behavior of the muscle.

The action current of muscle as well as of nerve is strong enough to have a stimulating action of its own (Matteucci). If the nerve of one muscle, B, be laid across the belly of another muscle, A, and the second muscle be then stimulated through its own nerve, with each contraction of A, B also contracts, and this even in case A is so tense that it no longer changes its form. The contractions of B agree minutely in number, strength and sequence with those of A. If A is tetanized, B also is tetanized. These phenomena are called *secondary contractions*, secondary tetanus, etc.

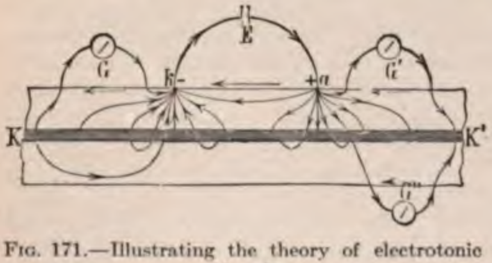

FIG. 171.—Illustrating the theory of electrotonic currents, after Hermann.

2. *Electrotonic Currents.*—When an electric current is conducted through a certain length of a medullated nerve and another portion of the nerve outside of this length is connected with the galvanometer, an

excursion of the needle is seen which indicates the presence of a current in the portion led off. This current is in the same direction as the current applied to the nerve (called the *polarizing current*), and is spoken of as an electrotonic current. The strength of this current depends upon many different circumstances; it is stronger, the less the distance from the portion of the nerve traversed by the polarizing current, and the stronger the latter is; moreover, the change (in the frog) is greater in the region of the anode than in the region of the cathode.

The electrotonic currents are branches of the polarizing current. According to Grünhagen, they arise because the inner parts of the nerve fibers, the axis cylinders, are better conductors than the medullary sheaths. Consequently the current (E in Fig. 171) spreads out over great lengths of the nerve, and when connection is made from these extrapolar parts with the galvanometer (G, G″), the threads of current break through to the surface. It may be fairly doubted now whether, as Hermann imagined, a polarization between the inner and outer parts of the nerve plays any part in producing these electrotonic currents.

B. THE MUSCLE TONE

If a person sticks his finger in his ear and then contracts his arm vigorously, he hears a dull sound, the pitch of which has been determined by Wallasten and others to be about thirty-two to thirty-six vibrations a second. Helmholtz observed that the same sound is heard very clearly if the ears (best at night) be stopped with drops of sealing wax and the masseter muscles be powerfully contracted. So long as the muscles remain at a uniform tension, one hears a dull, roaring sound, whose fundamental tone is not changed materially by increasing the tension, whereas the accompanying roar becomes both stronger and higher.

Helmholtz demonstrated further that the vibrations of voluntary muscles which produce the muscular sound do not occur so regularly as those of a musical tone, nor so rapidly as thirty-two to thirty-six per second. He found on the average only about nineteen per second. The muscular sound is therefore an overtone of the true muscle vibrations. Since the pitch of this sound changes also with the condition of the ear drum, it follows that the sound experienced is a resonance tone of the tympanic membrane, produced by the irregular concussions of the muscles. From these facts it is not difficult to understand why the simple contraction of a muscle produced by a single stimulus, and the systole of the heart as well, is accompanied by a muscular sound (cf. page 168).

C. THE CHEMICAL ALTERATIONS IN MUSCLE DUE TO ITS ACTIVITY

Active muscle acquires an *acid reaction*. This is probably due in part to an increased percentage of monophosphates, and in part to the formation of lactic acid. According to Helmholtz, working muscle contains less substance soluble in water and more substance soluble in alcohol than resting muscle. Again it is stated that in work the total quantity of creatin and creatinin increases and that of the xanthin bases decreases. Finally, the percentage of glycogen in the muscle diminishes.

An acid reaction has been observed in the neighborhood of the electrodes when nerves are stimulated. Since however no such change can be demonstrated at points of the nerve which have not been touched by the stimulating current, this acid reaction must be regarded as a direct effect of the current—i. e., *electrolysis*. Waller concludes from certain phenomena with the action current that the nerve forms carbon dioxide during its activity.

D. MECHANICAL WORK

The amount of mechanical work done by a muscular contraction depends primarily upon the strength of the stimulus, and upon the load.

1. *Effect of the Strength of Stimulus.*—If a muscle bearing a constant load be stimulated with a graded series of shocks beginning at a very low level and increasing slowly, it is found, both with direct electrical stimulation of the muscle and with mechanical or electrical stimulation of the nerve, that the height of the contractions increases more and more slowly with a uniform increase in the strength of the stimuli, and that it finally approaches its maximum after the manner of an asymptote (Fig. 172). The maximum shortening which can be obtained under the most favorable circumstances with a single contraction is about twenty per cent of the natural length of the muscle.

The muscular tension obtained with a maximal stimulus applied to the nerve is considerably smaller than that obtained by a maximal stimulus applied directly to the muscle itself (Dean). If this is true of the natural stimulation from the central nervous system also, it means that the muscles are always capable of more work than can ever, under normal circumstances, be obtained from them.

2. *Effect of Load with Constant Stimulus.*—We shall consider only the case of a maximal stimulus.

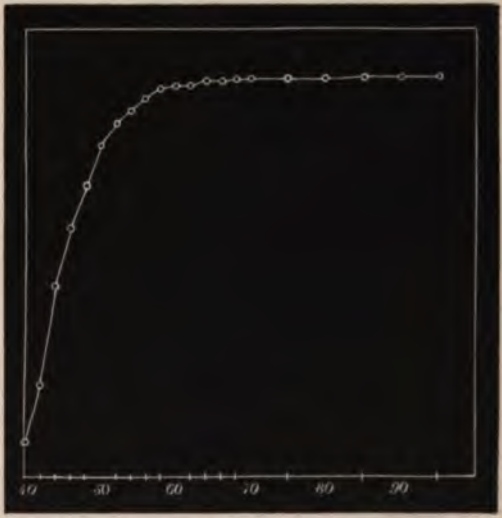

FIG. 172.—Frog's gastrocnemius. Stimulation of the nerve with break-induction shocks; load constant. The abscissæ represent the strength of the stimuli, the ordinates the height of the contractions.

One can vary the way in which the power of the muscle is taken up by making the contraction: (1) *isotonic*—i. e., where the load is constant throughout the contraction; (2) *auxotonic*, where the load increases constantly throughout; and (3) by *supporting the load* so that it is not lifted until the muscle has contracted a certain distance (after-loading).

A perfect *isotonic contraction* is probably never obtained. Even when the mechanical conditions of the experiment fulfill the requirements for isotony as completely as possible, the contraction is retarded at its beginning by the inertia of the masses to be moved, consequently the tension of the muscle is greater at the start than later.

We designate as *auxotonic contractions*, first those in which the muscle works against a stiff spring, where the tension naturally increases as long as the muscle continues to contract, and secondly, those contractions in which the tension of the muscle is purposely increased by retardation of the movement at its beginning. Here belong the so-called *simple projectile motion* (Helmholtz), in which the muscle lifts a weight fastened directly to its free end, and the *projectile motion with dead weights* (Fick), where the muscle pulls on a lever with balanced weights.

In Figs. 173 and 174 are given examples of some of the different forms of motion, namely: Fig. 173 *a*, an isotonic contraction, Fig. 173 *b*, a simple projectile motion, Fig. 174, projectile motions with dead balanced weights.

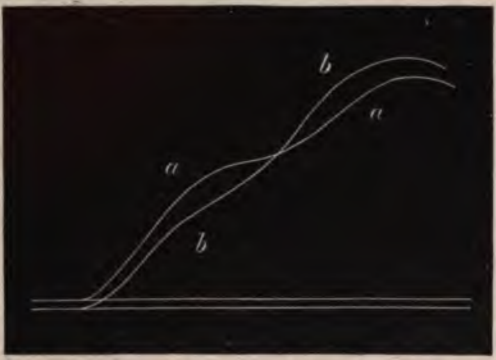

Fig. 173.—Frog's gastrocnemius. *a*, isotonic contraction; *b*, simple projectile contraction. Both were obtained with the same loads, 80 g., after Santesson.

In curves approximately isotonic, Fig. 173 *a*, as well as in pure auxotonic curves, which naturally reproduce the changes in length of the muscle most exactly, we find in the ascending limb a break, which is not an artifact but which, on grounds that cannot be discussed here, is probably due to the more sluggish contraction of the red muscle fibers (cf. page 416). In the projectile curve this irregularity does not appear, at least not so clearly, because the movement of the lever does not record the finer details of the contraction. The contraction produced by a single stimulus is, therefore, to a certain extent compound, owing to the fact that the different kinds of fibers composing the muscle become active at different times. In an exact analysis of muscular contractions, it is necessary to give this circumstance its proper weight.

Fig. 175 represents the single contraction of a muscle poisoned with veratrin, recorded on a slow-moving drum. Veratrin affects the red muscle fibers so that they contract much more slowly than is normal. The first rapid curve is referable to the white fibers, the second long-drawn-out curve to the red fibers.

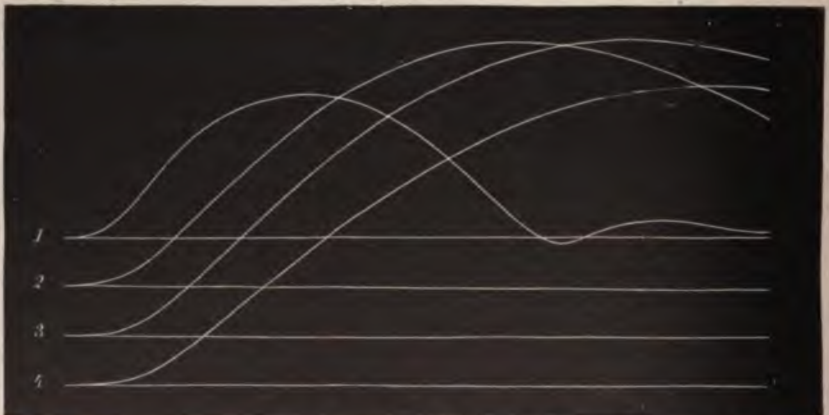

Fig. 174.—Frog's gastrocnemius. 1, loaded with 4 g., i. e., with the bare lever; 2, 40 g. dead weight; 3, 100 g. dead weight; 4, 200 g. dead weight.

After these preliminary remarks we can proceed with the discussion of the *effect of load* on the work of a muscle. We can say in general that the height of the contraction is less the greater the load. But this rule cannot stand without qualification. For under the isotonic arrangement we find the height less with a very light load than it is with one somewhat heavier (v. Frey), and under the purely auxotonic arrangement the height increases with the load up to a fairly high primary tension. Moreover, even if the height of the contraction does decrease as the load increases, it does so much more slowly than the load increases; so that up to a certain limit the work done (product of the load by the height of contraction) is greater, the greater the load (E. F. Weber).

Again, *an increase in the tension* of a muscle during its contraction has a decidedly favorable effect on its performance. Under some circumstances the contractions against a stiff spring are just as high or even higher than isotonic contractions obtained with a primary tension of the same amount (Santesson); and projectile contractions are sometimes higher than isotonic contractions with the same primary tension (cf. Fig. 173). Finally, cases have been recorded where auxotonic contractions which begin with the same tension are higher with a strong spring than with a weak one. We can say, therefore, that within certain limits the work done by a muscle is increased both by a higher primary tension and by an increase in the tension during the contraction.

In close connection with this comes the additional fact that under the isometric arrangement the increase in tension takes place much more rapidly than does the shortening under the so-called isotonic arrangement; or, in other words, its length remaining the same, the muscle reaches its maximum tension much earlier than it reaches its maximum shortening when the tension remains the same (Fick, Fig. 176).

A muscle appears therefore to have the *power of regulating the amount of work done* under a given stimulus, according to the requirements of the case. We must forego a complete theoretical discussion of these facts here; but we would direct attention to the significance of the red fibers in this connection. They are, as it appears, the most important source of the additional work done as the result of an increased tension. Thus we find that the secondary lift due to these fibers, in contractions against a tense spring in-

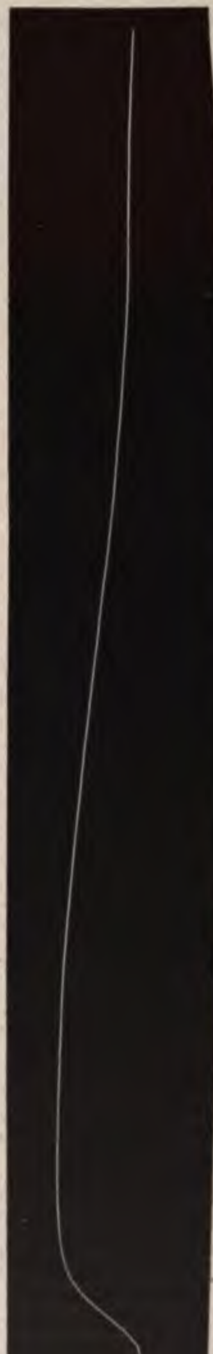

FIG. 175.—Contraction curve of a frog's gastrocnemius poisoned with veratrin, after Santesson.

creases as the tension rises, whereas the primary lift caused by the white muscle fibers, decreases as a rule with a rising tension (cf. page 436).

3. *The Absolute Power of a Muscle.*—The method of after-loading has been used for the purpose, among other things, of determining the so-called absolute power of the muscle. A muscle is loaded only with a lever, and the lever is supported mechanically so that the weights hung on it, which constitute the after-load, do not affect the muscle so long as it is resting. It is loaded by the weights only when contraction begins, and lifts them only when its tension overcomes the after-load. By adding weights one reaches finally a mass which the muscle no longer has the power to lift. This weight is taken as the absolute power of the muscle (E. F. Weber).

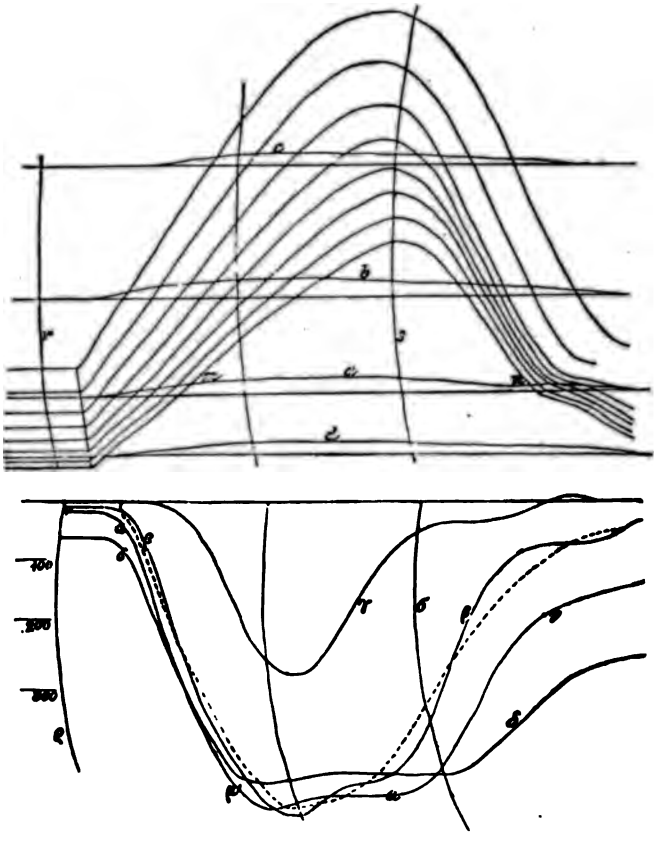

FIG. 176.—Isotonic (upper) and isometric (lower) contraction curves under the same primary tension, after Fick. To be read from left to right. The curves *a*, *b*, *c*, *d*, represent the shortening of the muscle corresponding to the isometric contractions α, β, γ, δ.

It is evident that, other things being equal, the absolute power of a muscle must be proportional to its cross section, or in other words, among muscles composed of the same kind of fibers the *thickest is the strongest.* In tetanus the absolute power is greater than in simple contractions, and for the voluntary contractions of human muscles it amounts, according to various authors, to 10 kg. per square centimeter of cross section.

If an experiment be so arranged that the muscle lifts its load after it has contracted to different heights, and the absolute power for these successive heights be determined, we find that it grows steadily less (Schwann's experiment).

4. *The Work of Tetanized Muscles.*—In tetanus it is evident that the work done after the tetanus has reached its full height is from a mechanical point of view nothing at all. Since, however, the contracted state always calls for an expenditure of energy, tetanus is accompanied by a relatively great consumption of substance, which in its turn leads to rapid fatigue.

The work of tetanus as related to its shortening is in general similar to that of a single contraction, only *it is more extensive*, so that under favorable circumstances the shortening may amount to as much as sixty-five to eighty-five per cent of the muscle's length. Moreover the ratio of shortening in tetanus to shortening in simple contraction is very different for different kinds of muscles; thus it is stated that the maximum shortening in tetanus of the white muscles of the frog is two to three times the maximum shortening in a simple contraction; of the red muscles eight to nine times.

The height of tetanus with a constant load depends on the strength of stimulus, but not upon the frequency of stimulation.

E. HEAT FORMATION IN MUSCLE

By employing the thermo-electrical method, Helmholtz (1847) demonstrated the formation of heat in the tetanus of the exsected frog's muscle. Later the production of heat in a simple contraction was demonstrated by Heidenhain. And Blix has shown that heat is formed even in resting muscle. Even with the most delicate methods *no heat production can be demonstrated in nerves.*

Since the performance of mechanical work and the production of heat are the two chief functions of muscle, and since, as we have seen above, the mechanical work done under a constant stimulus increases up to a certain limit with the load, it might be supposed that the heat production going on at the same time would be in inverse relation to the load, so that the dissimilatory process evoked in a muscle by a given stimulus would be independent of the load, and the latter therefore would influence only the apportionment of the total output of energy by the muscle to the two functions. But this is not the case. Since the investigation of Heidenhain, we know that *the total output of energy* in an exsected frog's muscle under a constant stimulus, *increases* up to a certain limit *with the load.*

This property of the muscle appears to be of very great importance. For if the total performance of the muscle were independent of the load and were dependent only on the strength of stimulus, the development of energy in the muscle might often be out of all proportion to the work to be done. The relationship discovered by Heidenhain is to be looked upon as a *regulatory mechanism* which, independently of the nervous impulses, controls the metabolism in the muscle according to its momentary needs (cf. also page 441).

Fick and his pupils have made absolute determinations of the amount of heat developed in muscular activity, and the amount of work done at the same time. Some of their results are brought together in the following table. In these experiments the load was allowed to fall again after each contraction, so that the observed quantity of heat expresses the total output of energy. Each experiment consisted of three maximal contractions following one another in rapid succession.

Load, g.	Heat-production in micro-calories.	Work, g. mm.	Thermal equivalent of work.	Ratio of work to heat.
0	14.6	....	....	....
20	18.3	465	1.09	16.7
40	19.7	802	1.88	10.5
80	23.9	1,420	3.34	7.1
120	24.2	1,914	4.50	5.4
160	25.8	2,402	5.64	4.6
200	25.6	2,905	6.83	3.7
160	26.2	2,402	5.64	4.6
120	23.3	1,914	4.50	5.2
80	21.9	1,430	3.34	6.6
40	19.5	819	1.92	10.2
20	18.0	465	1.09	16.6
0	13.4	....	....	....

We see that under a maximal stimulus and with increasing load the ratio of *work: heat* changes in favor of the former. With the least load the total production of energy is 16.7 times the amount of work done, whereas with the heaviest load it is only 3.7 times as much. In other experiments a still greater part of the total production of energy appeared as mechanical work. But as a rule in the frog's muscle cut out of the body by far the greatest part of the energy developed in contraction is used for the production of heat.

§ 5. THE CENTRAL INNERVATION OF A SKELETAL MUSCLE

Each one of the muscles of the extremities receives motor-nerve fibers from several successive nerve roots. This is most clearly seen in the case of the *sterno-cleido-mastoid* and the *trapezius* of man which are innervated by both the spinal accessory and the cervical nerves. This fact alone appears to indicate that under normal circumstances some of the fibers of a muscle are not thrown into action, but that the muscle has the power of *contracting partially*. The following experiment by Gad confirms this conclusion.

The lumbar plexus of the frog conveys nerve fibers to the gastrocnemius by two roots. If with a light load the muscle be given a tetanic stimulus directly or indirectly by one or by both of these roots the contractions are of equal size. But if the tension developed in the muscle in tetanus be studied by means of the apparatus figured on page 414, it is found to be less when the stimulus is applied to only one root than when applied to both or to the muscle directly, and that in the latter two cases the tension is equal to the sum of the tensions developed by separate stimulation of the two roots. The result goes to show that on stimulation of different nerve roots, not the whole muscle but only certain of its fibers are excited, or in other words that each nerve root produces a partial contraction. There can be no doubt that such partial contractions occur also normally under the influence of the nervous system, although probably with still nicer gradations. In this way the activity of the muscle is adapted to the work to be performed. If no great degree of tension is called for, only a few muscle fibers contract, the others remain quiet and do not become fatigued. Since on the other hand the extent of the contraction does not depend upon the cross section, but upon the length of the muscle, we may get just as much shortening with a partial contraction as when the whole muscle is active.

§ 6. FATIGUE AND RECOVERY OF MUSCLES AND NERVES

A. GENERAL PHENOMENA

If a *frog's muscle* be stimulated repeatedly with single shocks given every one to two seconds, at first its contractions increase in size, even if the stimulus remain of the same strength ("treppe" of Bowditch and Buckmaster), and then they gradually decrease until complete exhaustion is reached. From the first of the series the contractions become more prolonged, since both the ascending and the descending limbs of the curve, but especially the latter, occupy more time. As fatigue progresses and the longer stimulation is kept up, there gradually develops a new condition of the muscle: at the end of the contraction it does not return to its resting position but remains more and more shortened.[1] The muscle finally becomes a sluggish, stubborn mass yielding to the traction which strives to restore it to its original form, with extreme slowness (Funke). In the series represented in Fig. 177 a muscle kept perfused with blood was stimulated every 1.5 seconds. Only the first ten of every fifty contractions are here reproduced, the six series representing all told some three hundred separate movements. When the interval between stimuli is made still shorter, say 0.5 second, as fatigue continues the descending limb of the curve does not reach the base line, before it is met by the following stimulus, and the curve becomes much like an incomplete tetanus. With a longer interval, say six seconds, the contraction is not prolonged, or only slightly so, and the reduction in the height of the curve is the only expression of fatigue.

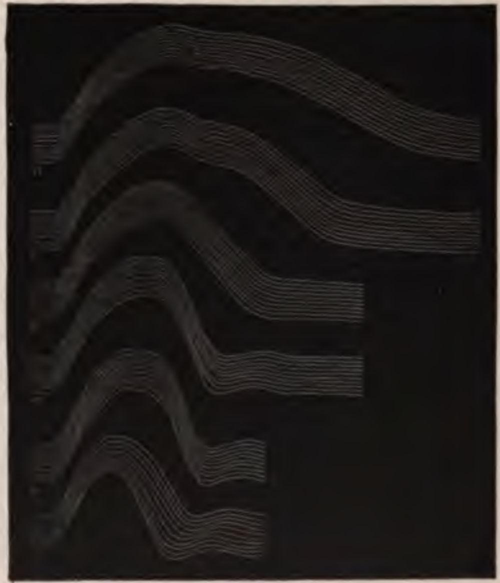

FIG. 177.—Changes in the character of the contraction produced by fatigue, after Rollet.

The *muscle of warm-blooded animals*, kept perfused with blood, show, according to Rollet, only this latter form of fatigue, with no material increase in the duration of the contraction even when the interval between stimuli is very

short. Consequently in these muscles the above-mentioned incomplete tetani are entirely wanting.

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[1] This condition is called contracture.—ED.

[According to F. S. Lee this difference in the mode of fatigue between the excised muscles of cold-blooded and of warm-blooded animals is due to a real physiological difference and not, as had been supposed by Schenck and Lohmann, to a mere difference of temperature. Lee finds that the muscles of the former exhibit the same characteristic slowing of the contraction process (cf. Fig. 178) both at low and at high temperatures (though at the high temperature to somewhat less extent than at the low); whereas the muscles of the latter do not exhibit this phenomenon at either high or low temperatures. "The poikilothermal condition (cf. page 46) is more primitive than the homoiothermal, and it would seem that the constant influence of a uniform temperature acting for ages on the skeletal muscles of warm-blooded animals has impressed on them certain pronounced peculiarities." Possibly the part which these muscles themselves play in the production of heat is in some way associated with this physiological difference. —Ed.]

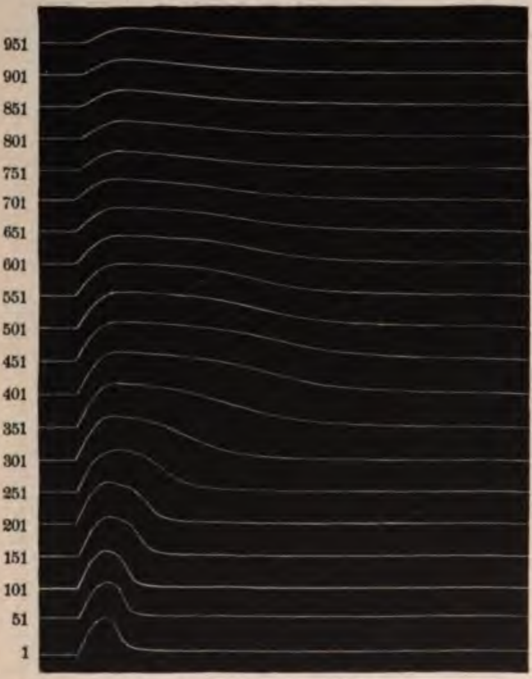


Fig. 178.—Isotonic contractions of a frog's gastrocnemius, after F. S. Lee, showing changes due to fatigue. Only every fiftieth contraction is recorded.

With regard to the fatigue of nerves we must distinguish very clearly between the *local fatigue* which takes place in artificial stimulation at the point where the stimulus is applied, and which in part at least is due to the injurious effects of the stimulating agent, and the fatigue which is *produced* possibly *by the transmission of stimuli.* Since only the latter determines the normal behavior of nerve, we shall discuss it alone.

In order to observe the fatigue of nerve, it is necessary to so arrange the experiment that its muscle is not stimulated. Bernstein fulfilled these requirements by stimulating the sciatic nerve of the frog a long distance from the muscle, at the same time conducting through the nerve between this point of stimulus and the muscle a strong constant current. The resistance at the anode of the constant current prevented the stimulus applied farther up from reaching the muscle. In this way Bernstein found that the nerve was much less capable of fatigue than the muscle. By the same method Wedensky was able to stimulate a motor nerve of the frog for six hours without exhausting it.

This same *resistance of nerves to fatigue* has been demonstrated also by Langendorff, Bowditch and others, on warm-blooded animals. If curare, which throws out of action the end plates of the motor nerves, be administered to an

animal, the poison will be gradually thrown off from the body, and the end plates will again recover their function. But several hours intervene, and a stimulus applied during the interval is of course without effect on the muscle. But when the poison wears off, the effect of stimulation returns with all its original force, which means that stimulation continued for hours has not fatigued the nerve. Brodie and Halliburton observed likewise that nonmedullated nerves, such as the splanchnic, were not fatigued by artificial stimulation lasting six hours.

Besides this any number of natural phenomena show that nerves have a much greater endurance. We know, indeed, that several efferent nerves, especially the vagus branches to the heart, are all the time under a tonic excitation of greater or less intensity, also that the same is true of the afferent nerves, examples of which we have in the constant pains of certain nervous maladies.

From these facts the conclusion has been drawn that nerves in general are not fatigued, and it cannot be denied that this conception is, to a certain extent, well founded. Nevertheless, one must not imagine that no metabolic processes are taking place in an active nerve or that it mediates the transmission of stimuli, as for example a wire does an electric current; such a supposition has little probability in its favor on purely antecedent grounds, for a nerve is a living tissue. Moreover, there are a number of direct observations at hand which show the presence of chemical processes in nerve with perfect definiteness.

For example, a nerve deprived entirely of oxygen becomes completely inexcitable within three to five hours, but recovers its excitability again within three to ten minutes when oxygen is supplied. This phenomenon as well as the production of carbon dioxide in active nerves (cf. page 434) substantiates the view that a nerve, so far as processes taking place within it are concerned, presents no essential difference from the other organs of the body. On the other hand its extraordinary resistance to fatigue presupposes a very low state of metabolism and a very great power of recuperation. This ability to recover is probably different also in different nerves; for in the olfactory nerves of the pike unmistakable signs of fatigue make their appearance after only a short period of excitation (Garten).

Contractions can still be induced by direct stimulation long after the muscle fails to respond to a tetanizing stimulus applied to its nerve. Since the nerve itself does not fatigue we must suppose that the nerve endings fatigue much earlier than the muscle substance itself (Waller).

B. FATIGUE OF HUMAN MUSCLES AND NERVES

The phenomena of fatigue in man have recently been studied by several authors by means of the ergograph, an apparatus first constructed by Mosso.

This *ergograph* is especially constructed for the flexion of the middle finger, and consists of two parts, one to which the hand is fastened and another which records the contractions of the muscle. The whole apparatus is shown in Fig. 179. The forearm is fixed in position by means of the clamps and the hand by means of the two tubes into which the index and ring fingers are thrust. A string fastened to the middle phalanx of the middle finger, carries the load and moves the writing lever. The latter records the contraction of the muscle, enlarged about twice, on a slowly rotating drum. The work of the muscle is of course the product of the actual height of contraction by the load.

If now the load be not too light and the interval between contractions not too great, the height continually declines until finally the subject is no longer

able to lift the load; but if the load be diminished, he can continue the work immediately. The fatigue curve either declines rapidly at first and more slowly at the end, as in Fig. 180, A, or the fall at the beginning is slight and is rapid toward the end (Fig. 180, B). Judging by Mosso's results every individual has his own peculiar form of fatigue curve.

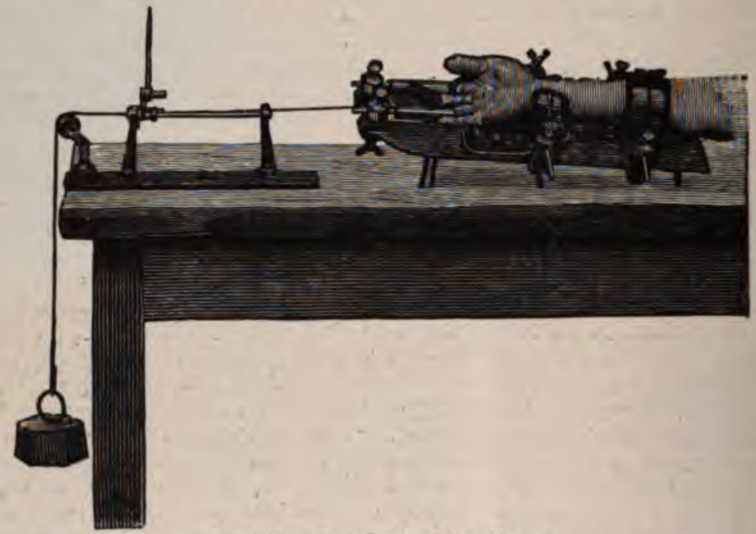
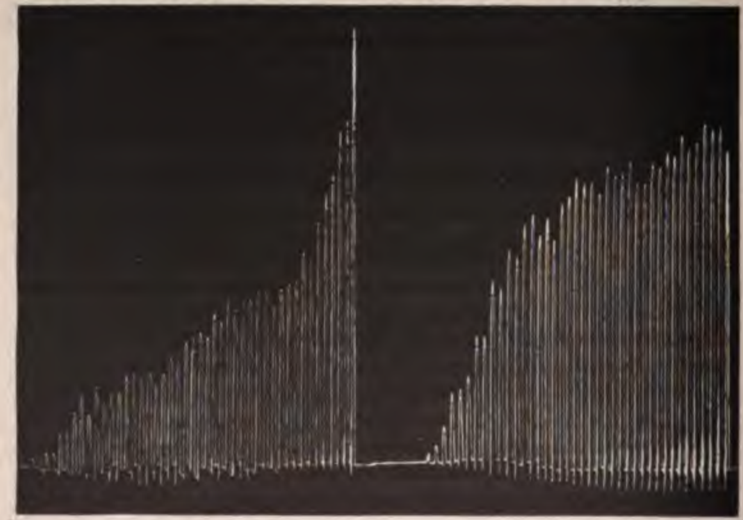


FIG. 179.—Ergograph, after Mosso.

Of the factors which influence the progress of fatigue we shall investigate first the effect of frequency of contraction with a constant load. Figs. 181, A to



A *B*

FIG. 180.—Fatigue tracings obtained with the ergograph of Mosso. To be read from right to left.

D show that exhaustion comes on more rapidly the smaller the interval between contractions. In Fig. 181, A we find only fourteen contractions before complete exhaustion, mechanical work = 0.912 kg. m. In Fig. 181, B the number of contractions is eighteen, and the mechanical work done 1.080 kg. m. In Fig. 181, C the number of contractions is thirty-one and the mechanical work 1.842 kg. m. With a rhythm of one contraction every ten seconds no fatigue at all appears (Fig. 181, D). An interval of ten seconds, therefore, is sufficient to permit a skeletal muscle to recover completely.

When a muscle is worked at a rapid rhythm to the point of complete exhaustion, it requires a rather long time to recover completely—in the experiments of Maggiora from one and one-half to two hours. It was also shown in these experiments that the last contractions of a series ending in complete exhaustion, are the most fatiguing. If only the first part, say the first fifteen contractions, of a fatigue series be carried out and rest be then permitted, the muscle will recover in a much shorter time proportionally than if it were completely fatigued. Consequently the total amount of work which can be done in a day is considerably greater if the muscles be not pushed at any time to the limit of their powers. For example, a muscle making fifteen contractions every thirty minutes for fourteen hours did mechanical work of 26.9 kg. m.; the same muscle when made to perform the whole series of fatigue curves every two hours accomplished a mechanical work of only 14.7 kg. m.; a difference of 12.2 kg. m.

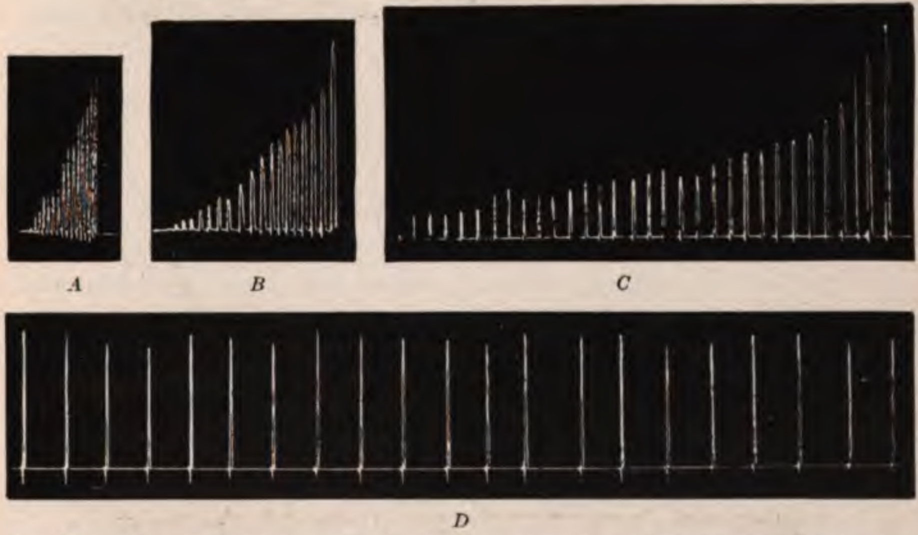


FIG. 181.—The onset of fatigue under stimuli of the same strength, given at different intervals, after Maggiora. *A*, once a second; *B*, once every two seconds; *C*, once in four seconds; *D*, once in ten seconds. To be read from right to left.

Anæmia, fasting, want of sleep, among other things, reduce the working power, and favor the onset of fatigue. The capability of work is increased, on the other hand, by rest, by taking food, and by massage—the latter even in case the muscle be previously not fatigued. The effect of massage after work therefore consists not only in the removal of products arising from the expenditure of energy, but also, and to a considerable extent, in the more active circulation of the blood and lymph and possibly in some alteration of metabolism thereby produced. Experiments on exsected frog's muscles indicate that there is a direct influence on the contractile substance (Ruge).

Fatigue of one group of muscles exercises an unmistakable influence on other muscles—e. g., fatigue of the legs hastens fatigue of the arms; but muscular training reduces such effects.

It has been shown also that purely mental work hastens muscular fatigue to a very great extent. It might be supposed that this part of fatigue is purely central; but the matter is not so simple. The same result is obtained where an artificial stimulus is applied to the median nerve or directly to the flexor muscles of a person fatigued by mental work.

Finally, by other experiments which cannot be described here, Mosso has shown that while the mechanical work performed by a muscle decreases as fatigue comes on, the *nervous effort* and the intensity of the processes which call forth the contractions progressively *increase*. By a method especially adapted to the purpose, it may even be shown that the nervous mechanism is being greatly strained before there is any sign of fatigue in the external work done. This, as Treves remarks, would explain the fact that athletes not infrequently are attacked by severe neurasthenic pains.

An increase in the output of CO_2 and in the consumption of O_2 is another characteristic of fatigued muscle; that is, the utilization of energy becomes more and more unfavorable with the progress of fatigue.

What has been said here concerning fatigue and recovery applies especially to the *skeletal muscles*. Other muscles fatigue much more slowly and require a much shorter time of recovery in order to remain permanently in functional condition. The best example of this is the heart, which throughout life works uninterruptedly with rest periods of only about 0.4 second. That the smooth muscles also are capable of long-continued work is shown by the tonus which they maintain in the arterial walls.

In view of the facts presented here it becomes a matter of interest to inquire under what circumstances the *greatest amount of muscular work* can be performed. This question cannot be answered fully at present, but we have some facts bearing on the subject which are of considerable interest. When one does the same amount of external work in two sets of experiments which differ only in the circumstance that the load and the distance through which it is lifted vary in reverse order (e. g., 20 kg. × 0.3 m. and 30 kg. × 0.2 m.) it is found that the fatigue comes on much more rapidly with the heavier load (Stupin). The conclusion is that the size of the load and not the absolute amount of muscular work done determines how long the movement can be continued. But if the load is too small the muscle evidently cannot accomplish much work. We may say, therefore, in general that the greatest quantity of work can be done when the load is of medium size.

This medium load may be found (Treves) by choosing a weight with which a person while perfectly fresh can do the greatest absolute amount of work and observing the record until the contractions exhibit evidence of fatigue. If now the weight be diminished so that the contractions of the same extent can continue, and so on, a weight will finally be found with which the person can continue the work at the same rhythm indefinitely.

The following table, compiled by Blix, contains some data on the maximal muscular capacity of man at different kinds of work:

KIND OF WORK.	Time.	Kg. m. per second.	Observer.
Climbing mountain and stairs...	8 hours	10.5	Weissbach
Turning crank	1½ hours	12.5	Sjöstrom
" "	15 minutes	17.0	"
" "	5 minutes	19.5	"
" "	1½ hours	27.7	"
Climbing stairs without load....	4 seconds	101.2	Blix
Climbing stairs with load.......	4.5 seconds	95.4	"

It is evident that the capacity for work calculated per second is greater, the shorter the total time occupied. The highest record of endurance yet made was observed in a six-day bicycle contest in New York. According to Atwater's calculation the victor performed during his first day of twenty-three hours and ten minutes an average of 25 kg. m. per second, and in the whole time, one hundred and eight hours and forty-four minutes, an average of 20.2 kg. m. per second.

§ 7. RIGOR MORTIS

A muscle cut out of the body or excluded from the circulation passes sooner or later (ten minutes to several hours) into a rigid condition known as the death stiffening or *rigor mortis.* It is now shorter, thicker and firmer, turbid, opaque and less extensible; its reaction is acid, probably owing to the transformation of a portion of the diphosphates into monophosphates brought about by the lactic acid formed.

Rigor of muscle is produced also by warming to 48°–50° C., by the effects of distilled water, by acids and by various other substances. It appears more readily after heavy muscular work than otherwise, but on the other hand appears later if the muscle has been paralyzed by section of its nerve. Rigor mortis is the cause of the rigidity of the body after death. Under certain circumstances, which have not yet been successfully imitated, the stiffening comes on immediately after death, so that the body becomes fixed in the position it had at the instant of death.

Rigor is regarded by most authors as *coagulation* of the muscle proteids. But the processes taking place in rigor are only partially explained in this way, for we do not even know definitely how the proteids obtainable from muscle plasma occur in the living muscle. Besides, the phenomena of coagulation in a muscle extract, and the rigidity brought about artificially by different reagents, present several points of difference from the natural death stiffening.

§ 8. SMOOTH MUSCLES

The most satisfactory smooth muscles for study are those whose fibers run parallel, like the *retractor penis* of the dog and the circular muscles in the stomach of the frog. The extensibility of such muscles is relatively great and the elastic after-effect is very considerable. A small weight acting for a long time

short. Consequently in these muscles the above-mentioned incomplete tetani are entirely wanting.

[According to F. S. Lee this difference in the mode of fatigue between the excised muscles of cold-blooded and of warm-blooded animals is due to a real physiological difference and not, as had been supposed by Schenck and Lohmann, to a mere difference of temperature. Lee finds that the muscles of the former exhibit the same characteristic slowing of the contraction process (cf. Fig. 178) both at low and at high temperatures (though at the high temperature to somewhat less extent than at the low); whereas the muscles of the latter do not exhibit this phenomenon at either high or low temperatures. "The poikilothermal condition (cf. page 46) is more primitive than the homoiothermal, and it would seem that the constant influence of a uniform temperature acting for ages on the skeletal muscles of warm-blooded animals has impressed on them certain pronounced peculiarities." Possibly the part which these muscles themselves play in the production of heat is in some way associated with this physiological difference. —Ed.]

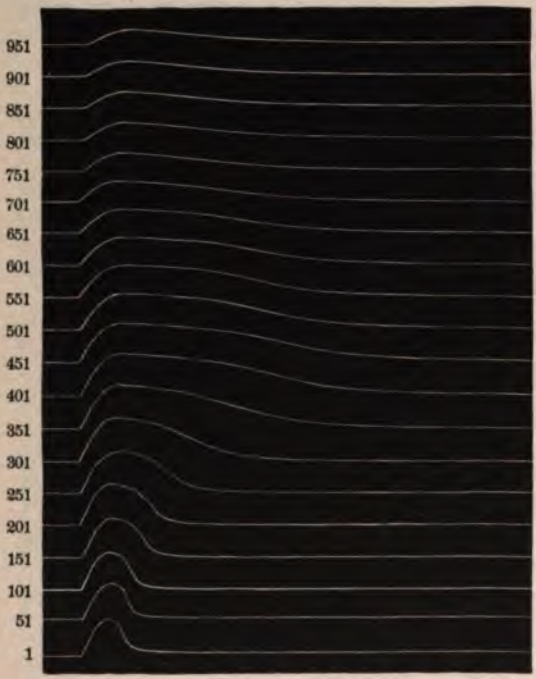


Fig. 178.—Isotonic contractions of a frog's gastrocnemius, after F. S. Lee, showing changes due to fatigue. Only every fiftieth contraction is recorded.

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B. FATIGUE OF HUMAN MUSCLES AND NERVES

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This *ergograph* is especially constructed for the flexion of the middle finger, and consists of two parts, one to which the hand is fastened and another which records the contractions of the muscle. The whole apparatus is shown in Fig. 179. The forearm is fixed in position by means of the clamps and the hand by means of the two tubes into which the index and ring fingers are thrust. A string fastened to the middle phalanx of the middle finger, carries the load and moves the writing lever. The latter records the contraction of the muscle, enlarged about twice, on a slowly rotating drum. The work of the muscle is of course the product of the actual height of contraction by the load.

If now the load be not too light and the interval between contractions not too great, the height continually declines until finally the subject is no longer

short. Consequently in these muscles the above-mentioned incomplete tetani are entirely wanting.

[According to F. S. Lee this difference in the mode of fatigue between the excised muscles of cold-blooded and of warm-blooded animals is due to a real physiological difference and not, as had been supposed by Schenck and Lohmann, to a mere difference of temperature. Lee finds that the muscles of the former exhibit the same characteristic slowing of the contraction process (cf. Fig. 178) both at low and at high temperatures (though at the high temperature to somewhat less extent than at the low); whereas the muscles of the latter do not exhibit this phenomenon at either high or low temperatures. "The poikilothermal condition (cf. page 46) is more primitive than the homoiothermal, and it would seem that the constant influence of a uniform temperature acting for ages on the skeletal muscles of warm-blooded animals has impressed on them certain pronounced peculiarities." Possibly the part which these muscles themselves play in the production of heat is in some way associated with this physiological difference. —Ed.]

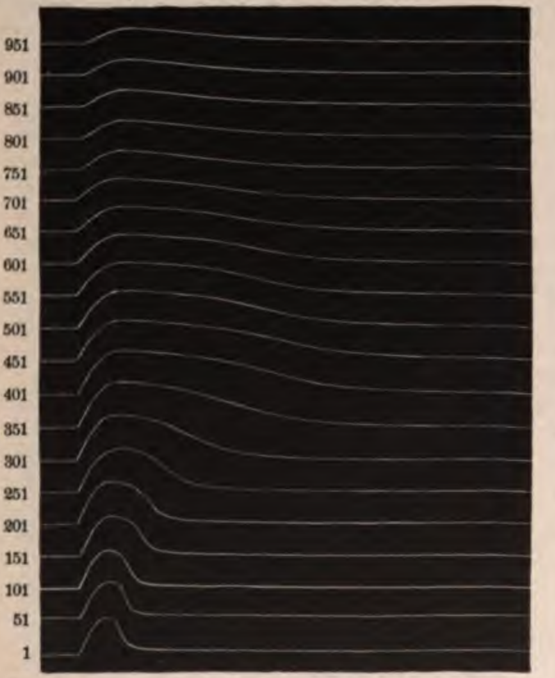

Fig. 178.—Isotonic contractions of a frog's gastrocnemius, after F. S. Lee, showing changes due to fatigue. Only every fiftieth contraction is recorded.

With regard to the fatigue of nerves we must distinguish very clearly between the *local fatigue* which takes place in artificial stimulation at the point where the stimulus is applied, and which in part at least is due to the injurious effects of the stimulating agent, and the fatigue which is *produced* possibly *by the transmission of stimuli.* Since only the latter determines the normal behavior of nerve, we shall discuss it alone.

In order to observe the fatigue of nerve, it is necessary to so arrange the experiment that its muscle is not stimulated. Bernstein fulfilled these requirements by stimulating the sciatic nerve of the frog a long distance from the muscle, at the same time conducting through the nerve between this point of stimulus and the muscle a strong constant current. The resistance at the anode of the constant current prevented the stimulus applied farther up from reaching the muscle. In this way Bernstein found that the nerve was much less capable of fatigue than the muscle. By the same method Wedensky was able to stimulate a motor nerve of the frog for six hours without exhausting it.

This same *resistance of nerves to fatigue* has been demonstrated also by Langendorff, Bowditch and others, on warm-blooded animals. If curare, which throws out of action the end plates of the motor nerves, be administered to an

animal, the poison will be gradually thrown off from the body, and the end plates will again recover their function. But several hours intervene, and a stimulus applied during the interval is of course without effect on the muscle. But when the poison wears off, the effect of stimulation returns with all its original force, which means that stimulation continued for hours has not fatigued the nerve. Brodie and Halliburton observed likewise that nonmedullated nerves, such as the splanchnic, were not fatigued by artificial stimulation lasting six hours.

Besides this any number of natural phenomena show that nerves have a much greater endurance. We know, indeed, that several efferent nerves, especially the vagus branches to the heart, are all the time under a tonic excitation of greater or less intensity, also that the same is true of the afferent nerves, examples of which we have in the constant pains of certain nervous maladies.

From these facts the conclusion has been drawn that nerves in general are not fatigued, and it cannot be denied that this conception is, to a certain extent, well founded. Nevertheless, one must not imagine that no metabolic processes are taking place in an active nerve or that it mediates the transmission of stimuli, as for example a wire does an electric current; such a supposition has little probability in its favor on purely antecedent grounds, for a nerve is a living tissue. Moreover, there are a number of direct observations at hand which show the presence of chemical processes in nerve with perfect definiteness.

For example, a nerve deprived entirely of oxygen becomes completely inexcitable within three to five hours, but recovers its excitability again within three to ten minutes when oxygen is supplied. This phenomenon as well as the production of carbon dioxide in active nerves (cf. page 434) substantiates the view that a nerve, so far as processes taking place within it are concerned, presents no essential difference from the other organs of the body. On the other hand its extraordinary resistance to fatigue presupposes a very low state of metabolism and a very great power of recuperation. This ability to recover is probably different also in different nerves; for in the olfactory nerves of the pike unmistakable signs of fatigue make their appearance after only a short period of excitation (Garten).

Contractions can still be induced by direct stimulation long after the muscle fails to respond to a tetanizing stimulus applied to its nerve. Since the nerve itself does not fatigue we must suppose that the nerve endings fatigue much earlier than the muscle substance itself (Waller).

B. FATIGUE OF HUMAN MUSCLES AND NERVES

The phenomena of fatigue in man have recently been studied by several authors by means of the ergograph, an apparatus first constructed by Mosso.

This *ergograph* is especially constructed for the flexion of the middle finger, and consists of two parts, one to which the hand is fastened and another which records the contractions of the muscle. The whole apparatus is shown in Fig. 179. The forearm is fixed in position by means of the clamps and the hand by means of the two tubes into which the index and ring fingers are thrust. A string fastened to the middle phalanx of the middle finger, carries the load and moves the writing lever. The latter records the contraction of the muscle, enlarged about twice, on a slowly rotating drum. The work of the muscle is of course the product of the actual height of contraction by the load.

If now the load be not too light and the interval between contractions not too great, the height continually declines until finally the subject is no longer

in sensations which are more or less present to the mind. Sensations by which we have knowledge of the position in space of our bodies and their members, also of the extent of their movements and the intensity of muscular contractions—in short, all those sensations which are comprehended as belonging to the sense of motion come under this class. The sensations from other internal organs like the heart, stomach, intestines, bladder, etc., also belong here. The latter are not sharply defined unless intensified by some special cause; then they sometimes become very painfully conspicuous. As a rule, however, they are wholly indefinite and contribute in consciousness only toward the general *state of feeling*, which not only varies greatly according to the nature of these vague sensations, but may very profoundly influence our whole being.

One of the most significant facts in connection with the physiology of sensation is that our conscious sensations do not arise in the organs to which the afferent nerves are distributed and to which the stimuli are applied. The sensation of sight, for example, is not in the eye, the sensation of sound is not in the ear, etc. The peripheral sense organs and the peripheral endings of afferent nerves in general are for the sole purpose of *transferring the stimuli* which strike them to the appropriate nerves. The nerves transmit the excitations thus aroused to the central organs of the nervous system and the conscious sensation arises only by the activity occasioned in the brain. Different parts of the brain are set in action directly, according as one afferent nerve or another is excited (cf. Chapter XXIII).

How can a material change in the brain give rise to a conscious sensation? Philosophers of all times have tried to answer this question. Since we are discussing it here only from the standpoint of natural science, we cannot enter into the philosophical considerations. It is likely, indeed, that the question can never be answered from the standpoint of natural science alone, for, as Du Bois-Reymond especially has pointed out, the question is at bottom a *metaphysical* one.

If our knowledge of nature were so far advanced that all the movements in the world could be resolved into the movements of atoms, and our explanation of nature could thus be reduced to the mechanics of atoms, we would of course be in a position to describe the material changes taking place in the brain in definite psychical processes very exactly. Satisfactory as this knowledge would be, it would nevertheless be unable to give us any conclusive information concerning the relation of such movements to such ultimate facts as: "I feel comfortable," "I feel pain," and the proposition immediately deducible therefrom: "I think, therefore I am." That is to say, it is impossible to conceive scientifically how consciousness and thought can arise out of the interplay of atoms. Indeed we could imagine a world similar to our own, in which everything would take place exactly as in our world, but where there were no consciousness and no thought; and yet the mechanics of atoms would be just as valid for such a world as for our own.[1]

In what sense do our sensations produced by external stimuli correspond to reality? Philosophy and natural science attack this problem from opposite sides and yet the two have the same task in common.[1] The former, which considers the psychical side, seeks to eliminate from the cognitive and perceptive processes everything which proceeds from the effects of the objective world, in order to obtain in its purity that which is proper to the mind itself. Natural science on the contrary seeks to remove the relative and the formal elements of thought, definition, notation, forms, hypothesis, etc., in order to secure what belongs to the world of actuality, the laws of which it seeks to know. In order to give a theoretical explanation of sensations from the scientific standpoint we must bear in mind the following propositions.

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[1] Cf. Du Bois-Reymond, "Limits of Our Knowledge of Nature," translated by J. Fitzgerald in Popular Science Monthly, May, 1874.

1. There are two different degrees of distinction among sensations. The one most essential is the distinction between those belonging to the different senses, as between the sensations of blue, sweet, warm, and loud. This difference is designated as the difference in *modality* of sensation, and is so complete that it precludes any transition from one to the other or any relation of greater or less similarity between them. For example, one cannot say whether sweet is more like blue or red. The second difference, which Helmholtz limits to a difference in *quality* between sensations belonging to the same sense, is less exclusive. Within the same sense transition and comparison are possible. From blue we can pass through violet and carmine red to scarlet red and can say, e. g., that yellow is more like orange than like blue.

We distinguish the following modalities: pressure and touch; heat and cold; taste; smell; hearing; and sight. (With regard to pain cf. Chapter XVII, § 4.)

2. Experiment has shown that the profound difference between the senses does not depend in any wise upon the kind of external stimuli by which the sensations are aroused, but is determined solely *by the kind of sensory nerve affected.*

For illustration, physics considers light as extremely rapid vibrations of a hypothetical, imponderable medium, the ether, which is distributed throughout all space. When these vibrations of the ether strike the retina, the latter is excited and in its turn produces through the optic nerve an excitation in the brain, which gives rise in consciousness to a sensation of light. But this sensation of light has not the least resemblance to the vibrations which constitute the objective phenomenon of light. This itself should be fairly convincing evidence that the sensation cannot agree in kind with its external cause. Conclusive proof is found in considerations such as the following: If the eyeball be pressed upon, we receive even in pitch darkness a sensation which is characterized by a brilliant play of colors. A blow upon the eye produces a flash of light. Here we have a perfectly typical sensation, and yet no light at all has reached the eye. The sensation is unquestionably due to an excitation of the optic nerve produced by the mechanical pressure on the eyeball. The same thing is experienced when an electric current is conducted through the eye; we get a sensation of light, even though no objective light may be present.

3. Since therefore sensations of exactly the same nature are aroused by three wholly different kinds of stimuli—light, mechanical pressure, and elec-

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[1] The following discussion is essentially a repetition of the views of Helmholtz as set forth in "Die Tatsachen in der Wahrnehmung," Berlin, 1879.

tricity—it is evident that the character of the sensation cannot agree in any way with the external cause by which it is produced.

This conclusion is confirmed by experiments demonstrating that one and the same external cause can produce entirely different sensations, by acting upon different sense organs. Thus, pressure on the skin gives a sensation of pressure or of contact; pressure on the eyeball a sensation of light. When illuminating rays strike the eye, we get a sensation of light; when the same rays, sufficiently strong, strike the skin, they produce a sensation of warmth. The sensation which is aroused by an electric current applied to the eye has an entirely different character from that which one gets when the current is applied to the skin.

4. Just as sensations have their *origin* in the brain, so also do they receive their *specific character* from the cerebral background. A sensation of light, however produced, is, in the last analysis, conditioned by a material change in the brain. It follows that such sensations may arise, when neither the eye nor the optic nerve is stimulated, if only the seat of sensation in the brain is excited in some way, as by a disturbance in the blood supply, etc.

Herein lies the cause of visual *hallucinations.* For our subjective experience it is a matter of indifference how this particular place in the brain is roused to activity, whether mediately by the optic nerve or immediately by some process in the brain itself. The sensation of light in the latter case must be just as real for the person experiencing it as a sensation produced in the normal manner by the action of light on the retina.

What we have said concerning the sensations of sight, will of course apply to those from other senses.

5. Although all our sensations inclusive of the organic sensations have their origin in the brain, they are not consciously referred to the brain, but are projected outward either to other parts of the body or to the surrounding space. Thus we refer the sensations of touch to the skin; the sensations of taste to the tongue; those of smell to the space around us, to the nose, or to the mouth; the sensations of sound commonly to the surrounding space, in exceptional cases to the ear; sensation of sight always to the outer world.

The information concerning the general condition of the body brought to the central nervous system, is likewise projected for the most part to different organs. This occurs most definitely in the case of pains and motor sensations; but other organic sensations also are referred to peripheral organs—e. g., the sensation of thirst to the throat, the sensation of hunger to the stomach, etc.

Sensations which give us the general feeling of bodily tone, or of good spirits are not projected to any definite organ. Neither are they referred to the brain; they represent rather a general peculiar condition permeating the whole body, which is present to consciousness as depression, vigor, indisposition, comfort, etc.

From all this it follows that in so far as the nature of our sensation gives us any information of the peculiar external agency by which it is excited, it constitutes a *sign* rather than a *picture* of that agency. A picture demands some kind of likeness to the thing pictured, but a sign need bear no resemblance to the thing signified. The only necessary relation between the two is that a given object, present under the same circumstances, shall always produce the same sign, and that unlike signs shall always correspond to unlike agencies.

To the popular understanding which assumes the complete truth of the pictures represented to us by our senses, this remnant of similarity may appear very meager. But in reality it is not so; for services of the greatest possible moment to us, such as the portrayal of uniformity in the processes of nature, can be performed for us by mere signs. Every natural law declares that conditions which are the same in a certain respect are always followed by results which are the same in a certain other respect. Since likeness in our world of sense is signified to us by like signs, the natural sequence of cause and effect will have its counterpart of a perfectly uniform sequence in the realm of sense. If therefore even the qualities of our sensations are nothing but signs which are entirely dependent in kind upon our nervous organization, they are not to be discarded as mere worthless counterfeits. They are signs *of something*, whether of something merely existing, or something occurring, and what is more important, they are able to portray to us the law of occurrence.

Physiology, therefore, acknowledges that the nature of sensation is, in the last analysis, subjective. In essence it is transcendental. But since experience proves that excitation of different afferent nerves produces different sensations, since we know further that sensation has its correlative physical process not in the excitation of the peripheral sense organ or that of the afferent nerves, but in the activity of the brain, and finally since investigation has shown that different afferent nerves terminate in different fields of the cerebral cortex, which in their turn are connected with other parts of the brain, it follows that the specific character of a sensation is determined by the part of the brain roused to action. It is in this sense that we shall understand the *doctrine of specific sensations*, as used in this book.

SECOND SECTION

THE QUANTITATIVE RELATIONS BETWEEN STIMULUS AND SENSATION

In order that an external stimulus may produce a sensation, it must exceed a certain lower limit of strength, which is called, after Herbart, the *threshold value* of the stimulus.[1] If the stimulus be increased above this limit, the sensation increases also; but while the strength of the external stimulus may be increased indefinitely the intensity of the sensation never exceeds a certain upper limit. This maximum sensation follows a relatively weak stimulus and a further rise not only does not produce a quantitative increase in the sensation but on the contrary and in ascending degree produces fatigue and exhaustion of the peripheral sense organ.

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[1] The threshold value of the stimulus for the different modalities of sensation varies greatly according to circumstances. In absolute terms it may be given as follows: for the sensation of pressure $\frac{1}{10.000}$th of an erg; for sensations of sound $\frac{1}{10.000.000}$th of an erg; for sensations of sight (green) $\frac{1}{100.000.000}$th of an erg.

Between the minimum and the maximum, as thus defined, variations in the strength of the stimulus will produce variations in the intensity of the sensation.

§ 1. WEBER'S LAW

In estimating differences in the intensity of sensations we meet with a peculiar difficulty. We can say that a certain sensation is stronger or weaker than another of the same kind, but we cannot say *how much* stronger or weaker it is; for every sensation constitutes a whole in itself and cannot be represented as the sum of several individual sensations. If, for example, a white surface is illuminated at one time by 1 candle power and at another by *n* candle powers, we can say perhaps that the sensation in the second case is stronger than in the first; but we cannot tell how much stronger it is.

The relation between the strength of the stimulus and the intensity of the sensation is not to be determined by merely setting arbitrary stimuli over against the sensations evoked by them. We can better approach the problem by inquiring *how much a given stimulus must be changed* to produce a perceptible change in the intensity of the sensation. E. H. Weber who made the first observations along this line (1831) laid down the following law known by his name: *The increase in the stimulus necessary to produce a perceptible change in a given sensation must always bear the same relation to the size of the initial stimulus.*

Thus, if to a weight of 1 unit a person must add a weight of $\frac{1}{20}$th in order to make the second load perceptibly heavier in his own subjective appreciation of weight than the first, then, according to Weber's law, with an initial load of 10 the superadded weight must be $\frac{10}{20}$ths to enable him to detect the difference.

By placing weights on both hands at the same time, the hands being supported on the table, Weber found that the "threshold difference" was one-third of the initial stimulus, but when the same hand was successively weighted it was only one-fourteenth to one-thirtieth of the initial stimulus. In estimating weights by the muscular sense—i. e., by lifting them—the threshold difference goes down to one-fifteenth to one-twentieth when both hands are used simultaneously, and to one-fortieth when the weights are lifted successively with the same hand.

According to experiments by Merkel with fairly pure pressure stimuli, the threshold difference for 50, 100, 200, 500 and 1.000 g. was $\frac{1}{17.9}$, $\frac{1}{15.6}$, $\frac{1}{18.5}$, $\frac{1}{20}$, and $\frac{1}{17.5}$ respectively. For weights above and below these values it is not so constant.

Another illustration of the law is the following: When one looks at a drawing with shadings under different degrees of illumination, the fine gradations of brightness come out with about the same clearness. For example, if he look at the drawing first with the naked eye, then through a gray glass which diminishes the intensity of the light rays from different parts of the drawing to the same extent proportionally, the different parts of it are still seen in their proper relations as regards light and shade. This would not be true if the same proportional decrease in the intensity of the stimuli coming from different parts of the drawing produced proportionally different variations in the resulting sensations. It is owing to this same peculiarity of our organ of vision that we do not see the stars in daylight. The amount of light which the stars contribute to the illumination of the heavens is too slight in proportion to the total illumination for us to detect them.

Merkel has shown that the same law holds for the sense of hearing, and Camerer and Kepler for the sense of taste.

Weber's law is true within fairly wide limits for all the senses, but for very high or very low degrees of intensity certain variations come in. However, since the stimuli of medium intensity are the ones that occur most commonly in our everyday life, we may say that in general our estimates of differences in intensity follow this law.

In attempting a theoretical explanation of Weber's law it must not be forgotten that the conscious sensation aroused by an external stimulus occurs only when the excitation begun at the sense organ reaches the cerebral cortex. It is possible that in the purely physiological events taking place in the peripheral sense organ, in the nerves and in the central nervous system a certain increase in the stimulus produces the same absolute increase in the excitation aroused. If so, the relationship expressed in Weber's law would be due to something which is peculiar to the process of arousing a conscious sensation from a physiological excitation. But it is also conceivable that the peripheral sense organ, nerves, etc., themselves react in accordance with Weber's law, and that the law is therefore a purely physiological one. The latter alternative is probably correct, for approximately the same relationship of excitation to intensity of stimulus has been observed in many purely physiological processes.[1]

References.—*W. James*, "Principles of Psychology," New York, 1905.—*O. Kulpe*, "Outlines of Psychology," translated by E. B. Titchner, New York and London, 1901.

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[1] Fechner sought to deduce from this law of Weber a more general one, known as the psychophysical law. By giving the former an algebraic expression and using the differential calculus he arrives at the formula $E = C \log. \text{nat.}\ r$. (where E is the sensation, C a constant, and r the stimulus), which means that the sensation is proportional to the natural logarithm of the stimulus. So many objections have been urged against this formulation that its further consideration here seems unwarranted by its importance for the physiological side of the questions involved.—Ed.

CHAPTER XVII

THE SENSORY FUNCTIONS OF THE SKIN

ASIDE from serving as the outer covering of the body and in addition to what it does in the service of heat regulation, the skin has very important sensory functions. Notwithstanding that much has been explained by work done within the last decade, the intimate mechanism of these functions still appears to be very enigmatical. We shall divide them into three different groups, namely: (1) sensations of temperature, (2) sensations of pressure and touch, (3) sensations of pain.

§ 1. SENSATIONS OF TEMPERATURE

Temperature sensations are of two kinds, *cold and heat sensations*, and both are probably related to the regulation of heat in our bodies. The nerves which mediate these sensations produce reflex effects, which manifest themselves as variations in the intensity of combustion, in the distribution of blood, and in the activity of the sweat glands. The conscious sensations of temperature inform us how the thickness of our clothing and the temperature of our rooms need to be changed one way or the other, although it must be allowed that this information not infrequently leads us astray.

Until a few years ago it was generally supposed that the diametrically opposite sensations of heat and cold were mediated alike by all parts of the skin and that only one kind of nerve fibers was concerned in both sensations. Blix and Goldscheider independently of each other (1883, 1884) demonstrated, however, that not all points on the skin are capable of arousing temperature sensations of both kinds, but that the nerves which mediate sensations of heat have their end organs at different points from those which mediate sensations of cold.

This proposition is proved by the following experiments. A metallic tube drawn out to a fine point is filled with water of the desired temperature. When cold water is used and the tip of the tube is applied to the skin, care being taken not to exert pressure, one observes that the point can only be felt cold at certain spots, while at others it produces no sensation of temperature at all. If the experiment be repeated, using this time warm water instead of cold, we find that sensations of heat can be received only from certain points.

Marking off cold spots and heat spots on the skin with different colors, we find that the two do not coincide, although it must be said that a perfectly exact determination of their relative positions is very difficult or quite impossible, owing to the conduction of heat by the skin (cf. Fig. 182).

The presence of different temperature points has been established not only by use of the appropriate temperature stimuli but also by mechanical, electrical and chemical stimulation.

The sensation which is produced by stimulation of a single temperature point is not "pointlike"; instead, one experiences a sort of irradiation of the feeling, so that the sensation is more extensive than the temperature point —i. e., it appears to be disklike and at the same time to have depth. It is on this account that the temperature sensations aroused by contact with warm and cold objects appear to be perfectly continuous, giving no indication of the pointlike arrangement of the end organs. Then we are inclined also to fill up unconsciously all the gaps in our special sensations (cf. the blind spot in the eye, Chapter XXI).

The number of cold spots in the skin of an adult is found to be 6–23 per square centimeter of surface; the number of warm spots 0–3. The entire surface of the body would contain, therefore, about 250,000 cold spots, and about 30,000 warm spots. In a child the temperature points appear to stand closer together, and this may be taken to mean that the child is born with his complete equipment of such points.

In order to obtain a more accurate idea of the topography of the temperature senses, Goldscheider has stimulated different portions of the skin with the ends of cold and hot rods 3–4 cm. in diameter. One cannot obtain the number of temperature points by this method, but can test the relative sensitivity of different regions very well. Thus if there be no temperature points in a certain portion, application of the rods will produce no sensation of temperature at all; if points are present, they may vary both in number and excitability, so that the degree of sensitivity will vary. A surface with only a few *intense* points would give a stronger sensation than another with many *weak* points, etc. Fig. 183 is given as an example of the topographical distribution of the cold and heat senses.

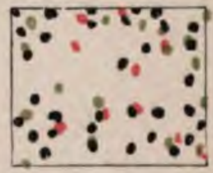


FIG. 182.—The arrangement of cold spots (green), heat spots (red), and pressure spots (black) on a small area of the dorsal side of the left wrist, after Blix.

Goldscheider summarizes his numerous experiments on this subject as follows: (1) The cold sense is everywhere more perfectly developed both extensively and intensively than the heat sense. (2) This relationship holds as well for the parts of the skin habitually clothed as for the parts habitually naked. Goldscheider finds the cause of this regional difference in the varying number of nerve fibers supplied to the different places. Of course there should be added also the varying thickness of the epidermis covering the end organs.

The experiments of different authors agree fairly well with regard to the acuteness of the temperature senses in the different regions. Those most sensitive to temperature stimuli are the nipples, and the breast in general, the alæ nasæ, the anterior parts of the arm; then follow the outer angle of the eye, the upper lip, the abdomen, the volar side of the forearm, the inner parts of the thigh, the foreleg, etc. Least sensitive of all is the scalp.

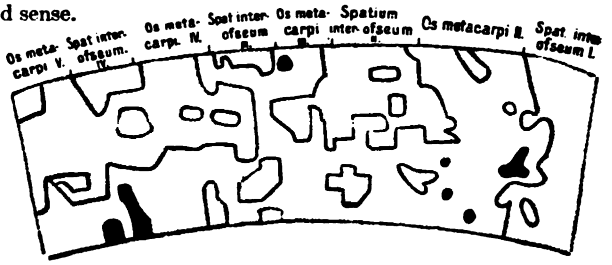
The hand is but slightly sensitive to temperature and in general it can be said that those regions of the skin which are used especially for touch are less sensitive to temperature than other regions.

The temperature sense is about equally developed at symmetrical points on the two sides of the body, but there is no special congruence exhibited between such points.

The mucous membranes possess as a rule but a feebly developed temperature sense, or, as is true of the cornea, none at all. Especially is the heat sense poorly developed in such places.

A given cold stimulus will evidently produce a greater cooling in a unit of time and will therefore constitute a stronger stimulus for the cold nerves, on parts of the body which are ordinarily clothed than on unclothed parts. The relation of the heat sense to the cold sense is for this reason somewhat different on clothed and unclothed parts.

a. Cold sense.



b. Warm sense.

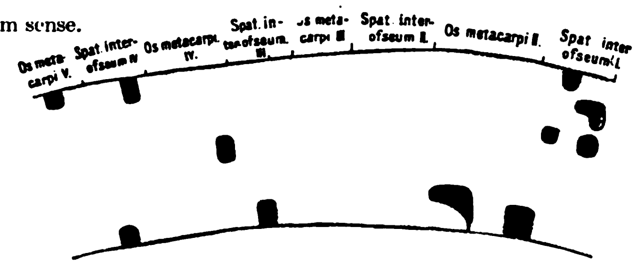


Fig. 183.—Topographical distribution of the cold and heat senses over the middle region of the back of the hand, after Goldscheider. The relative sensitivity is indicated by depth of shade.

So long as the temperature of the surrounding atmosphere changes but little, we do not as a rule experience any sensation of temperature, although some parts of the skin, according as they are clothed or not, may be very much warmer or colder than others. When a person goes from one room in which he feels neither cold nor warm into another which is colder (or warmer), he immediately feels cold (or warm). But if the difference between the two rooms is not very great, all sensations of temperature disappear within a short time. If now he returns to the first room, his experience of temperature will be just the reverse of the former change, until again the sensation gradually wears off.

The temperature of the surrounding atmosphere therefore may vary within certain limits without producing in us any corresponding sensation. One might suppose that this ability of the skin to adapt itself to slight changes of temperature would be due to variations in the distribution of blood, so that the end organs would have a uniform temperature in spite of the variations outside. But this is not the case, for Thunberg has shown that the adaptation is to be observed even after a large quantity of blood has been drawn from the vessels.

E. H. Weber, to whom we owe the first careful studies on the sensory functions of the skin, was of the opinion that the heat spots are stimulated specifically by an increase in the temperature of the skin and the cold spots by a fall. Hering, on the other hand, conceives that the determining factor is not the temperature of the skin but of the thermal apparatus itself. We cannot here enter into a discussion of the merits of these two hypotheses. We may merely mention one phenomenon which can scarcely be explained by either of them.

It is a common experience that one sometimes feels a *sensation of chill on getting into a hot bath.* This is because the cold spots of the skin respond to the heat stimulus with their own peculiar sensation. Excitation of these spots by heat occurs only with stimuli of 45° C. and upward (Lehman, v. Frey). The reverse process of stimulating the heat spots by cold gives no reaction.

The end organs of the temperature nerves share with other nervous end organs a peculiar property, in virtue of which the strength of the excitation aroused depends upon the rapidity of the stimulation, in this case upon the rapidity of the increase or decrease of temperature. The *strength of the sensation* depends also upon the size of the skin area stimulated: if the whole hand is dipped into water at 37° C. the water feels warmer than water at 40° into which only one finger is dipped.

If a piece of metal at 2–3° C. be placed in contact with the skin of the brow for, say, thirty seconds and then removed, the sensation of cold on that part of the skin is experienced for some twenty seconds afterwards (E. H. Weber) —i. e., the temperature sensation *persists* after the stimulus is removed.

A *change in the temperature* of the skin reduces the excitability of both kinds of temperature nerve endings. If one hand be held in moderately cold water and the back of the other hand be dipped in the same water, it seems colder to the latter hand. If the skin be overheated then dipped in cold water the water seems warmer than otherwise.

If *hot and cold stimuli be applied simultaneously* to the same skin area the sensation of cold appears first. Likewise on stimulation of the cold spots the sensation is sharper and reaches its maximum sooner than the sensation aroused by stimulation of the heat spots. This difference is not observed on stimulation of the temperature spots by electricity. From these facts v. Frey concludes that the heat endings lie in the deeper layers of the skin, the cold endings in the more superficial layers.

§ 2. PRESSURE AND TOUCH

By the pressure sense we not only distinguish pressure and contact, but learn also whether the surface of an object is smooth or rough, whether an object is sharp or dull, hard or soft, solid or liquid, etc. Here belong also itching and tickling sensations and the like.

It is perfectly certain that these different sensations are not all mediated by the true nerves of pressure, but that other afferent nerves play an important part. If for example, we perceive an object to be hard, this sensation of hardness is caused not only by the effect produced on the nerves of pressure, but there is experienced also a *sensation of resistance* which is evoked by the so-called *motor sense* (cf. Chapter XVIII). Since, however, these different kinds of pressure sensations have not been sufficiently differentiated either physiologically or psychologically, we shall limit the following discussion to pressure sensations in their simplest form.

Blix was the first to demonstrate by mechanical stimulation of the skin with fine points, that the pressure sense like the temperature sense is not continuously represented over the entire skin, but that the end organs of the nerves mediating the sensation of pressure are separate from one another and are not identical with the end organs of the temperature nerves (see Fig. 182).

Stimulating the pressure points as lightly as possible with a bristle produces a delicate but vivid and often somewhat tickling sensation, such as is experienced when one of the fine hairs on the skin is moved. According to Kiesow this shows that the *tickling sensation* is a sensation of pressure of a peculiar shade occurring under special conditions (and in certain cases connected with sensations of contraction). With a little stronger pressure the sensation takes on a perfectly characteristic quality, as if it were produced by a small, hard grain being pushed into the skin, hence the name "granular" used by Goldscheider.

The pressure spots can be sought out also by means of *induction shocks.* By monopolar stimulation of the spots a prickling sensation is experienced with a strength of current which gives no sensation at all if applied in the intervals between the spots. v. Frey, who has studied exhaustively the electric stimulation of the pressure points, observes that induction shocks produced by as many as 130 interruptions of the primary current per second are felt as independent shocks, also that the constant current causes a discontinuous excitation. On certain regions of the skin (fingers, tip of tongue, red edges of lips), Sergi has found that mechanical shocks can still be appreciated as distinct if they occur at intervals of 0.001–0.002 second.

The pressure points are arranged *with special reference to the hairs.* Each hair has a pressure point near its point of exit and directly above the deepest part of the follicle (v. Frey). It cannot be said however that the number of pressure points coincides exactly with the number of hairs. In the first place the hairs often stand in twos and threes and then are so close together, that it is not always possible to demonstrate the presence of pressure points belonging to them. Besides, one finds here and there within the regions clothed by hairs some pressure points standing quite apart and wholly unrelated to any hair.

The number of pressure points varies in different parts of the skin—e. g., on the flexor surface of the wrist 28 per sq. cm., on the anterior surface of the foreleg 5 per sq. cm. (Kiesow). According to v. Frey's estimate, the entire surface of the adult body, with the exception of the head, would probably contain about 500,000 pressure points.

Excitation of the pressure points appears to be accomplished by deformation of the skin. When a perfectly uniform pressure is applied to the skin no sensation is produced, the best illustration of which is the fact that we do not feel the pressure of the atmosphere. The following experiment also, first made by Meissner, illustrates the same point. If the hand be dipped into water or mercury at the temperature of the skin, no sensation is produced in any part of the skin submerged so long as the hand is kept perfectly still and contact with the vessel is avoided. But a sense of pressure is felt at the boundary line between air and liquid.

A weight allowed to rest upon the skin for a long time, is felt continuously, but with less and less distinctness as time goes on. Should the weight be very small, it may be felt only at the moment of its application. Removal of the weight is not of course appreciated unless it is heavy enough to be felt all the time it is present. Often the sensation outlasts the stimulus, probably owing to the persistence of the deformation in the skin.

Kiesow gives the following data with regard to the sensitiveness of the different parts of the skin. The relative strength of the tetanizing induction current necessary for the threshold stimulus is: on the tip of the tongue, 1; lips, 1.1; anterior half of the tongue, 5; tips of the fingers, 14–17; tip of the thumb, 19–21; edge of the kneepan, 21; styloid process of the ulna, 34–37.

Stimulating the skin of the frog with pressure, Steinach was able to observe an action current in the corresponding nerves, the strength of which was found to depend upon that of the stimulus.

§ 3. THE LOCAL SIGN

A person pricked on the skin with the point of a needle can tell with the eyes closed exactly where the needle is applied. This ability to refer a cutaneous stimulus to the correct place is often described for brevity as the sense of location, but is better described as the *power of localization*. E. H. Weber, who was the first to investigate this sense with any completeness, applied the two points of a draughtsman's compass to the skin and determined the least distance from each other at which they could be distinguished by the subject as two distinct points when applied to different parts of the skin. The less this distance was found to be the greater was the ability of the skin to localize the stimulus accurately.

The following are some of Weber's results, given in millimeters: tip of the tongue, 1; tips of the fingers, 2; lips, 4.5; dorsal side of the third joint of the fingers, 7; side of the tongue, 9; outer surface of the eyelids, 11; dorsal side of the first finger joint, 16; brow, 23; back of the hand, 31; sternum, 45; middle of the back, 68.

We see that the distance is greatest on the trunk and decreases more and more as we pass toward the ends of the extremities. It is least on the tips of the fingers (neglecting the tip of the tongue)—i. e., just where the skin is used for the most delicate touch and where the discernment of slight intervals between objects is most necessary.

Our ability to distinguish slight intervals of space with the skin is, however, not quite so limited as it might appear. In the first place as we know from many experiences, it can be *improved by practice*; in the second place slight intervals are much more sharply distinguished, if the two places on the skin are stimulated not simultaneously, but *successively* (Judd, v. Frey); and in the third place, this ability is much greater when two isolated pressure points are stimulated than when the needles are applied, as in Weber's experiments, quite at random. Under suitable conditions of the experiment the smallest distance at which any two stimuli applied to the skin can be recognized as distinct, corresponds closely with the distance, as determined by successive stimulation, of neighboring tactile points from each other (v. Frey and Metzner).

The differences already observed between different points of the skin, obtains also for the stimulation of isolated pressure points, as the following summary will show. The smallest perceptible distance for the nail joints, volar side is 0.1 mm.; for the balls of the fingers, 0.1–0.2 mm.; palm of the hand, 0.1–0.5; ball of the thumb, 0.2–0.4; nose and chin, 0.3; back of the hand, 0.3–0.8; cheek, arm, brow, 0.4–1.0; foreleg, abdomen, 1.0–2.0; thigh, 3.0; back, 4.0–6.0 mm.

It has been found also that the smallest perceptible distances are shorter when the points applied simultaneously are placed in the transverse direction from each other than when the line joining them lies in the longitudinal direction of the part, and that they decrease with the distance of the points tested from the axis of rotation of the members; thus, on the arm *above*, 53.8 mm.; *below*, 44.6; on the forearm *above*, 41.2; *below*, 22.5; on the hand *above*, 20.4; *below*, 7.8; on the third finger *above*, 7.5; *below*, 2.5 (Vierordt).

The power of localization is reduced by fatigue, anæmia, low temperature, etc., and is intensified by hyperæmia of the skin. Children have a more precise power of localization than adults.

It is really very remarkable that we have the power to distinguish two points as two when they are applied to the skin simultaneously. For the mere excitation from the one must be just like that aroused from the other. But the fact that we have the power to feel them as two must mean that the two sensations of pressure differ in some definite property. Since now we can distinguish simultaneously stimulated points better the farther they are apart, it follows further that this difference between the sensations produced from different points is greater, the farther they are apart.

This difference between the resulting sensations which enables us to locate the place of stimulation is known, since Lotze, as the *local sign*. Since every sensation arises in the last analysis through cerebral processes, we may conceive of the local sign as a difference in some property of the different sections of the brain, excited by stimulation of the different pressure nerves. In a crudely schematic way we may imagine that every pressure nerve is connected in some way with a special nerve cell and that excitation of this nerve cell produces a specific shade of sensation which differs from all other sensations of pressure.

The temperature nerves of the skin likewise possess this power of localization, but it is not so highly developed for temperature as it is for pressure. The cold spots appear to have a more precise power of localization than the heat spots.

The power of localization of the retina, especially of the fovea centralis, will be taken up in Chapter XXI.

§ 4. PAIN

If too strong a stimulus be applied to the skin or if it be continued too long or be repeated too often, a peculiarly disagreeable sensation, which we call *pain*, is aroused. With a sufficiently strong stimulus the sensation is diffused in our perception more or less beyond the part of the skin directly excited. And from pain of very great intensity convulsions, loss of consciousness, or even mental derangement may result.

Sensations of pain, whose important function it is to direct our attention to all kinds of influences, which, if neglected, might bring us into great danger, are mediated not by the skin alone, but by all other parts of the body as well. Pathological processes in the internal organs of the body or in its members are often accompanied by pain. Cramps of the muscles give rise to severe pains, and the feeling of great fatigue in the muscles after severe work lies on the borderland of painful sensations. Pressure on the eye causes pain, a bitterly cold wind causes pain. Then there are toothache, earache, headache, labor pains, and many others of which we have no need to be reminded.

It is very difficult to draw a sharp line between actual pain and a mere feeling of displeasure. High tones, e. g., are extremely unpleasant; so also are vibrations and rapid variations in the intensity of light; bad-smelling and bad-tasting substances produce nausea. Several of these and other analogous sensations produce in certain individuals effects quite similar to those of pronounced pains.

Only the painful sensations aroused by the skin have been subjected to exact analysis.

The cutaneous pains are not always of the same character, but exhibit differences which are due mainly to different combinations of the various sensations mediated by the skin, but also to the extent and duration of the stimulus. Thus a *burning* pain is accompanied by a sensation of heat; in a *stinging* pain the disturbance is confined to a small area of the skin; we call a pain *cutting* if it is distributed over some extent of the body with a certain speed; a *throbbing* pain is aroused when the pain comes and goes with the pulse, as, e. g., in the case of inflammatory pains, where the pulsations cause an increase in the pressure of the tissue.

Pain, more than any other sensation, has immediate reference to oneself, and likewise the intensity of pain more than that of any other sensation is influenced by the mind. When a person cuts himself *accidentally* with a knife, the cut produces no pain worth mentioning even though the wound be a deep one. But let him know beforehand that a slight operation, be it nothing more than a prick of the finger for a blood count, is to be performed on him, and it may cause him real agony. From this it follows that the *imagination of pain* increases its intensity very greatly.

By directing the attention very intently to a certain part of the body, a person may evoke creeping sensations, sensations of tension, pressure, etc., due to the dilatation of the arteries with the cardiac systole, to pressure of the clothes, etc., which otherwise he would not be conscious of at all, and by continued attention to them they gradually become more and more unpleasant and, finally, actually painful.

In diseases accompanied by pain, the pain is often more severe at night than during the day. This is probably due to the fact that in the daytime our attention is distracted by many things outside ourselves, and is not directed so exclusively to the body.

By purposely fixing one's attention on a definite object or idea it is possible to suppress not only the expression of pain, but to a large extent the pain itself. The following story of Immanuel Kant is much to the point. Kant suffered from time to time with attacks of gout which, as many know, may be very painful. "Out of patience at feeling myself deprived of sleep," he writes, "I soon seized upon the stoical expedient of fixing my thought intently on some chance object, whatever it might be (e. g., on the many ideas associated with the name of Cicero), and of consequently diverting my attention from all sensations. In this way the sensation speedily became blunted, so that the natural tendency to sleep overcame them. And this I could repeat with equally good results each time in the little interruptions in my night's rest occasioned by recurring attacks. But in the morning the shiny redness of the toes of my left foot was sufficiently convincing to myself that these sensations had not been purely fanciful."

Although all men have not the same will power as Kant had, we may nevertheless learn from his example that it is possible actually to suppress pain to a certain extent, just as it is possible for us to accustom ourselves to bear a necessary pain without sounding it abroad with loud wailings.

The expression of pain, therefore, is not to be accepted as a measure of its intensity. A strong-willed person may feel very severe pain without wincing, while another may cry out at a pin prick. On the other hand, we must not forget the experience oft confirmed in animals as well as in men that sensitiveness to pain is very different in different individuals. And since nobody can tell with certainty how strong is the pain which another feels, we ought not to withhold our sympathy from others when they give expression to pain.

It is very difficult to decide just wherein lies the *real physiological cause of pain*. Since we know that the pain aroused by any adequate stimulus has an altogether different character in different parts of the body—as, e. g., those aroused by a high temperature differ from those aroused by a low temperature, as the pain of muscle cramps is of a different kind from that of high pressure inside the eye, and the pains occurring in inflammatory processes differ according to the organ inflamed—the assumption is undoubtedly suggested that pain is produced by an excessive excitation of the ordinary afferent nerves from different parts of the body.

The fact that in certain diseases of the nervous system the sensations of pain are lost while the ordinary tactile sensations do not suffer any considerable diminution, does not militate against this hypothesis. One might readily imagine that the maximum excitation necessary for the production of pain were not reached, although the threshold stimulus remained approximately the same; and this supposition could be brought into line with Schiff's observation that section of the gray matter of the spinal cord abolishes sensations of pain without affecting the tactile sensations.

Proceeding from this observation it has repeatedly been conjectured that painful impressions are conducted through the gray matter, and that the sensations of pain are aroused by a sort of summation taking place in the cells of the gray matter, and there is any number of observations at hand which show that tactile stimuli, of themselves wholly painless, produce severe pain if repeated frequently enough. Likewise the irradiation of pain, as well as the occurrence in pathological processes of many accessory sensations of a painful character, appear to speak for the participation of the gray matter.

While these and other observations can be explained on the ground that the sensory cutaneous nerves already discussed mediate the sensations of pain, they do not, however, constitute positive proof of that proposition. Let us see what we may learn from investigation of the different sense points of the skin.

There prevails among authors who have busied themselves with this question a most gratifying agreement on one point, namely, that neither stimulation of the temperature points by their appropriate stimuli nor mechanically (by a needle thrust) produces any pain (Goldscheider *et al.*). Likewise when a heat spot is tested with very warm water, it gives a burning hot sensation but no pain. The heat pain might be regarded therefore as a separate sensation of pain merely colored by the excitation of the heat nerves, unless we suppose that the analgesia of the heat spots is due to the fact that the surface stimulated is too small; for it is a well-known fact that the size of the surface stimulated is a very important factor in the production of pain.

Blix demonstrated that on many parts of the body a needle can be thrust deep into the skin without producing any pain. The nerves which mediate pain therefore do not occur everywhere in the skin. Neither Blix nor Goldscheider however felt impelled to assume the existence of special nerves of pain with their own end organs, but conceived that sensations of pain have their origin in excitation of pressure nerves. v. Frey, on the other hand, entered the lists for special pain nerves and adduced the following weighty reasons, among others, for their existence.

(1) By observing certain precautions, mechanical stimulation of the skin with a bristle produces a pure sensation of pain without any preliminary or accompanying sensation of pressure. (It will be readily understood that the pain spots cannot be stimulated singly by mechanical means when they lie in the immediate neighborhood of pressure points.)

(2) If a bristle be placed over a pressure point, the sensation appears immediately, but at once fades away again and usually becomes unnoticeable after a short time. Over the pain point the effect appears later, gradually increases in strength and decreases again after reaching a maximum. If the sensation is still present after the stimulus has ceased, it disappears slowly. Intimately connected with this behavior is the fact that rapidly repeated electrical or mechanical stimuli (from five per second upward) applied to the pain point fuse as a rule into a continuous sensation, whereas through the pressure point we can distinguish very well 130 shocks per second (page 462).

(3) When the head of a pin is pressed for a moment into the skin, there follows very often after the sensation of pressure and separated from it by a short interval, a second sensation which is painful. Only pain points in the neighborhood of pressure points exhibit this phenomenon. On isolated pressure points the painful after-effect is wanting, and on isolated pain points the sen-

sation of pressure accompanying the stimulus fails, while the painful after-effect appears very vividly.

With regard to the topographical distribution of the pain spots we learn from v. Frey and others that on the back of the hand over the metacarpus of the ring finger 16 pain points, as against 2 pressure points, can be demonstrated within 12.5 sq. mm.—i. e., 1.3 pain points to the square millimeter.

From reasoning which we need not enter into here v. Frey has reached the following conclusions with regard to the anatomical structures which may possibly serve as the end organs of the different cutaneous nerves:

(1) Among the well-known sensory nerve endings on parts devoid of hair there is only one form which occurs in sufficient number to fulfill the requirements of an end organ of the pressure points, namely, the *tactile corpuscles* of Meissner. According to this discoverer there are—e. g., over the metacarpus of the little finger in 1 sq. mm. one to two of these corpuscles—which agrees well with the number of pressure points in the same place.

(2) These corpuscles however are quite exclusively confined to the parts devoid of hair. Anatomical investigations have brought to light the presence of a *wreath of nerve fibers* encircling the hair follicles down close under the opening of the sebaceous glands, their terminal processes penetrating the walls of the follicle as far as the glassy layer. This wreath of nerve fibers which occurs with the greatest regularity in every hair follicle may be the end organ of the pressure points associated with the hairs.

(3) The sensation of pain is probably aroused by stimulation of some mechanism lying nearer the surface. Since only free intraepithelial nerve endings are found external to the tactile corpuscles, we may look upon these as the organs of the (superficial) sensations of pain in the skin.

(4) Finally, v. Frey and Thunberg, the latter by careful analysis of the different phenomena attending stimulation with heat, have made it probable that the end organs of the heat nerves lie deeper than those of the cold nerves, also that the latter lie deeper than the end organs of the pain nerves.

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CHAPTER XVIII

ORGANIC SENSATIONS

WE include as *organic sensations* all those sensations aroused independently of external stimuli by internal processes going on in the various peripheral organs. Sensations excited from the sense organs normally by external agencies or abnormally by pathological processes evidently do not belong in this category.

Among the sensations thus defined we may mention first those which constitute the source of our general bodily feelings (page 452). But analysis of this class of sensations has not progressed far enough as yet to entitle them to further consideration here. We should mention also certain occasional sensations of pain arising within the internal organs concerning the exact cause of which nothing positive is yet known.

The only organic sensations thus far studied critically are those by which we form ideas of the *position* of our bodies and their parts (head, trunk and extremities) in space, and those by which we are made aware of the extent, intensity and direction of our *movements*. These sensations play a considerable part in the regulation of our movements and besides are very important in the psychological elaboration of our sense impressions (even of those which arise through external agencies), although they appear as a rule to be indistinct and indefinite in comparison with the last named.

The two groups of organic sensations just mentioned are not, however, everywhere sharply distinct from one another. The impulses by which we are made aware of our bodily movements, their direction and intensity, merge into the less distinct afferent impulses by which we form ideas concerning the orientation of our bodies. The anatomical substratum of our *motor sensations* and of our *sense of position* is furnished in part by the sensory nerve endings of the muscles, tendons, joints, skin and in part by those of certain portions of the inner ear (semicircular canals and otolith sacs).

§ 1. MOTOR SENSATIONS

Even with the eyes closed we have a very definite idea of the position of our limbs. If, for example, one arm be passively placed in a certain position, the person can with his eyes closed place the other arm in exactly the same position. Likewise a person has a perfectly precise idea with respect both to direction and speed of the changes in the position of his limbs. Finally, one can estimate weights very accurately by lifting them.

These and other similar sensations are described by different authors by different names, such as *motor sensations, muscular sense, sense of force,* etc.

This difference in terminology alone is evidence that views differ greatly as to the real cause of these sensations. According to some authors, like Ch. Bell and E. H. Weber, they are produced by excitation of the sensory nerves to the muscles; others, like Lotze and Schiff, conceive that they are evoked by the different foldings of the skin incidental to different positions; according to Bernhardt the sensory nerves of the skin, of the fascias and of the periosteum as well as the nerve trunks running through the muscles occasion muscular sensations; Lewinsky seeks their cause in the excitation of the nerves of the joints and bones; and many authors like Leyden, Meynert, Nothnagel and others assume that several different kinds of afferent nerves have a share in their production.

As for lifting an object with the hand, in a great majority of cases we send an impulse to the muscles which is exactly suited to the purpose, being neither too weak nor too strong. That is, if the object is a familiar one, we can adjust the voluntary impulse very exactly to the work to be performed. From this the conclusion has been drawn that the *feeling of effort* is the all-important thing in the perception of active movements (J. Müller, Wundt).

As a matter of fact it is easy to show that we do associate immediately with a voluntary impulse an idea of the movement as if it were already performed. Persons who have suffered amputation of a leg assert very positively that when they will to bend the lost part they experience a distinct feeling that muscles are being contracted.

But the central feeling of effort, however important it may be, is not the only determining factor. The mere development of our ability to adapt the necessary motor impulses to the lifting of different objects, involves the constant participation of afferent impulses which keep us informed of the results of the impulses sent out. It can be shown also without difficulty that the result of a voluntary impulse is usually controlled by afferent impulses. Thus, if we misjudge the weight of an object—e. g., overestimate it—we give too strong an impulse, as a consequence of which the object is lifted considerably higher than we intended it should be and we are immediately aware of the fact even without the use of our eyes. Similarly we are aware of the fact, if the impulse is too weak. Naturally if these afferent impulses participate in bringing about active movements, they must be the more necessary for making us aware of passive movements.

Let us see what are the afferent nerves mediating motor sensations. Anatomical proof of the presence of *afferent muscular nerves* has been furnished by Reichert, Kölliker, Odenius and others. We know too from the perfectly definite sensations of fatigue as well as from the pains of muscle cramps that these nerves are unquestionably able to mediate conscious sensations. They also give rise to reflexes, among which those producing vasodilatation and those involving the skeletal muscles as answering organs are the most important (Tengwall). It seems probable therefore that these nerves do play a prominent part in the motor sensations.

In the case of the eye muscles the afferent nerves are of great importance. We shall see later (Chapter XXI) that we have a very delicate appreciation of the slightest contraction of the eye muscles. This could only be true, if afferent nerves from the muscles or their tendons were present.

Likewise the thyroarytenoid muscle, whose finely graduated contractions determine the pitch of the vocal tones, appears to possess a very delicate muscular feeling produced by the afferent nerves; there is, however, no feeling of movement connected with this.

According to the view which Goldscheider in particular has worked out, the most important nerves for the perception of passive movements are the *afferent nerves of the joints.* The sensations of pressure and tension in the soft parts of the limbs not only do not produce the sensation of movement, they even interfere with it. Again, since the threshold value of the sensation —i. e., the smallest passive movement which one can perceive—is not influenced in any way by the degree of contraction of the muscles when the passive movement begins, coöperation of the muscular sensibility as a factor appears to be excluded. Finally the distance described by the moving force bears no relation to the amount of sensation which one experiences; the determining factor is the amount of rotation at the joint.

Lewinski made some experiments on ataxic patients (cf. page 472) by moving their limbs very slowly and very slightly at the ankle, knee and hip joints, part of the time pressing the parts together at the joint, part of the time not. When the parts were thus pressed the patients always perceived the movement very exactly, when not they could form no idea of the motion.

The *perception of active movements* likewise results from the rotation of the joints. To this are to be added, however, as contributing factors the sensations connected with the tension of the tendons and their epiphyses, possibly also the sensations aroused through the sensory nerves of the muscles. These sensations concern not merely the tendons, etc., of the active muscles, but also their antagonists. In a passive movement the tendons simply follow the pull; some are stretched, others are only under the tonic resistance of their own muscles.

In active movements, especially if the joint to be moved is loaded, we also experience sensations of *weight* and of *resistance.* The nerves of the joints and of the tendons are again of the first importance, the pressure on the surface of the joints and the tension of the tendons varying according to the resistance or the weight.

Jacobi has called attention to still another circumstance to which he ascribes great importance in the determination of the size of a weight, namely, the comparison of the amount of nerve force employed with the latent period of the movement—i. e., the time which elapses between the act of volition and the inception of the movement. The latent period, in his opinion, depends upon the amount of nerve force employed, and with the same amount of nerve force is proportional to the size of the weight.

The *sensory nerves of the skin* appear commonly to be of but slight importance in any kind of motor sensations. The sensation of weight remains unchanged after the skin is rendered insensitive to touch. And yet cutaneous sensations appear to contribute something to the quantitative refinement of a sensation of resistance as well as to the localization of the sensation and so to the formation of a clearer total impression (Goldscheider and Blecher).

In the case of the *face muscles* and the *levator palpebræ superioris* distinct sensations which inform us of the displacements suffered by the soft parts accompany the contractions (Goldscheider).

The sensations which make us aware of the *position of the extremities* have their origin in the skin, tendons, and probably the joints. By combination with *optical* memory pictures they give us our idea of position. Sensibility of the muscles appears to have little to do with the perception of position in the case of the extremities, but in the case of the eye muscles it plays a very important part.

§ 2. PHYSIOLOGICAL SIGNIFICANCE OF THE MOTOR SENSATIONS

Taken in their broadest sense, the motor sensations are of very great importance for the *regulation* of all bodily movements. Whenever any part of the body suffers loss of the motor sensations or a decline in their intensity and fineness, that part of the body exhibits disturbances in the coördination of its movements. In this way are brought about those pathological symptoms which are described as *ataxia* and which are defined in brief as a disturbance in the harmonious and purposeful coöperation of the muscles.

One of the most frequent forms of ataxia arising from lesion of afferent pathways is locomotor ataxia occurring in *tabes dorsalis*. It is characterized by the peculiar way in which the legs are swung and the feet planted in walking. Instead of the slightly flexed position of the normal leg as it is swung forward, the knee is extended, sometimes excessively, and the leg is thrust forward, the heel being planted on the ground with a sudden stamp. At the same time the legs are kept far apart, the trunk sways back and forth, and the body is in momentary danger of losing its equilibrium.

Coördination of the muscles being necessary to hold the body erect no less than to carry out movements of the limbs, ataxia is at times noticeable in standing. Thus ataxic persons are inclined to place the legs far apart in order to increase the area of support. If the feet are placed close together the body sways, or may fall, especially if the eyes be at the same time closed so as to shut out control by visual impressions (Leyden and Goldscheider).

There are many clinical observations to support this dependence of exact movements upon different impulses, and they are confirmed in the most beautiful way by experiments on animals.

Thus, after section of the afferent roots which supply one hind leg, a dog is unable to run on the ataxic leg when the sound leg is tied up (Hering, Jr.). When the afferent roots to both hind legs are cut, a dog is utterly unable to walk, and can only pull himself along on the abdomen by means of the fore legs, the hind parts dragging. Gradually, however, the dog can learn to walk again, and at the end of three to four weeks but few signs of the original disturbance are left (Bickel). There is therefore a means of compensating the loss of these afferent impulses.

J. R. Ewald observed that in cases of this kind the animal could call into play certain aids not previously used for regulation of his movements, and in fact Bickel observed that a dog which has recovered the use of his legs after an operation, exhibits again the original symptoms when he is taken into a dark room; from which it appears that the *optical apparatus* constitutes the compensating medium. H. Munk found on monkeys that after section of all the nerves to one anterior extremity, the insensitive arm could be extended for food on the same day of the operation, but the hand could not be moved. During the following days the number and extent of isolated movements steadily increased (more rapidly so with practice), and in a few days the animal could again grasp bits of food and convey them to its mouth. After some months the arm was used for almost all isolated acts, but continued to be more impulsive and cumbrous in its movements than the normal arm, which as time went on came to be used first on most occasions. The associated movements of the arm in walking, jumping, climbing, etc., however, were entirely, or almost entirely obliterated; at all events they were no longer used to any advantage.

We may sum up by saying that the messages conveyed by the afferent fibers to the central organs are of great importance not only for the coördination of movements but for the movements themselves, and that this depends primarily on the fact that it is through these messages that the individual learns to what extent the intended movement was carried out or failed to be carried out. The nerves of the organ itself are the ones most directly concerned, but they can be replaced to a greater or less extent by other nerves—as, e. g., the optic. When this compensation also fails the motor disturbance is greater than ever and it is conceivable at least that if all afferent impulses were completely inhibited, purposeful motor functions would no longer be possible.

§ 3. THE SEMICIRCULAR CANALS AND OTOLITH SACS OF THE INNER EAR

Physiological experiment and clinical experience both seem to have shown definitely that the afferent nerves of the *semicircular canals* and *otolith sacs* in the internal ear convey impulses to the nerve centers, which have much to do with the perception of position or changes in the position of the head as well as with other processes of *orientation*, etc.

We shall investigate these phenomena without for the present raising the question of how far the impulses give rise to conscious sensations.

A. ANATOMICAL

It is not our intention to describe the internal ear fully in this place; we shall only mention briefly the structural relations which are important for our present purpose. The internal ear can be divided into two portions, the *cochlea* and the *semicircular canals*, together with the *sacculus* and *utriculus*. These two divisions have as a matter of fact entirely different functions.

The cochlea unquestionably represents the end organ of those nerve fibers the excitation of which arouses auditory sensations, particularly those of musical tones. This is especially well borne out by the facts of comparative anatomy. In fishes the cochlea is represented only by a very small knoblike appendage to the saccule called the *lagena*. In frogs and toads the cochlea reaches a somewhat higher development and in the reptiles a regular progression of stages can be followed from the turtles and snakes to the lizards and crocodiles. In the last named for the first, and in birds the cochlea becomes curved and slightly spiral, while in the mammals it reaches its highest development by growing out into a long tube which describes upon itself one and one-half to four spiral turns.

The semicircular canals are arranged in the *three dimensions of space.* Inasmuch as the physiological investigations of these structures relate mainly to the pigeon, we shall describe them for this animal at once, following the work of J. R. Ewald. We find on each side of the head an *external*, an *anterior* and a *posterior canal* (Figs. 184 and 185). The two external canals lie almost exactly in the same plane, which when the head is in its normal position with the beak slightly lowered, is approximately the horizontal plane (Fig. 184). The planes of the posterior canal of one side and the anterior canal of the other are almost exactly parallel, but the projection of each is about 7 mm. distant from the other (Fig. 186) and each forms an angle of about 45° with the median vertical plane of the head. This relationship being true for both pairs (the left anterior with the right posterior, and the right anterior with the left posterior), it follows that the six canals together mark out three planes which lie in the three dimensions of space.

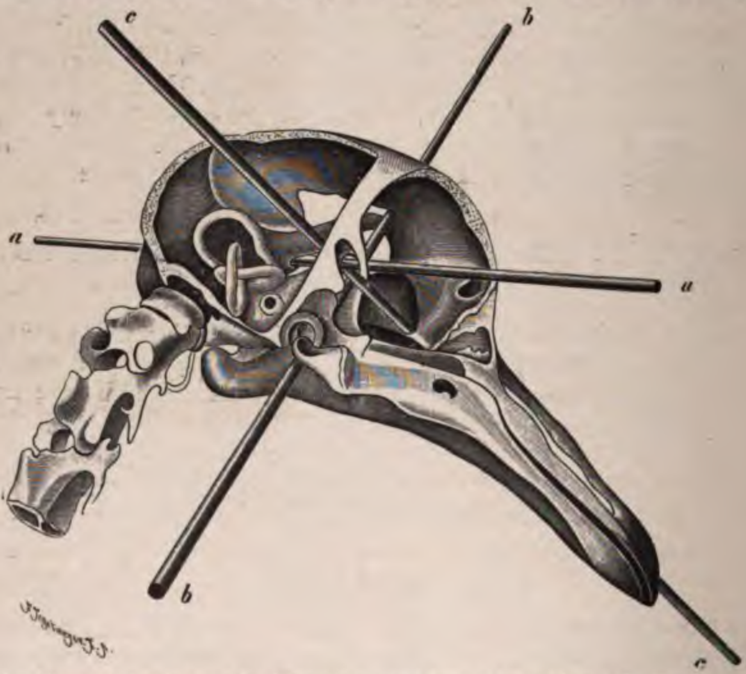

FIG. 184.—The semicircular canals of the pigeon laid bare *in situ*, after J. R. Ewald. The rods *a*, *b* and *c* are placed in the axes of the eyes, the skull and the beak.

This description applies strictly only to the middle portion of each canal, for its ends deviate somewhat from the course taken by the middle.

Each canal bears at one end an enlargement, the *ampulla*, which contains in its *crista acustica* the nerve endings of the canal. The ampullæ of the two canals which lie in the same plane are so arranged that particles moving in the same direction in the two move toward the ampulla of one and away from the ampulla of the other.

In the *sacculus* and *utriculus* likewise are nerve endings contained in the *maculæ acusticæ*.

These nerve endings consist of cells with hairlike processes, which in turn are connected with the terminal filaments of the eighth cranial nerve. In the ampullæ the hairs are bound together by a substance which is probably slimy and gelatinous in life. This substance, however, does not reach down to the epithelial surface, but is separated from it by a small space filled with endolymph, through which the hairs project before entering the slimy material. A small solid body, the so-called *otolith*, rests upon the hairs in each of the maculæ acusticæ. All vertebrates from the bony fishes up, with the exception of the mammals, have three otolith organs on each side (one in each of the three parts: utriculus, sacculus and lagena); the mammals have but two, since in them the lagena is absent, having been developed into the auditory cochlea.

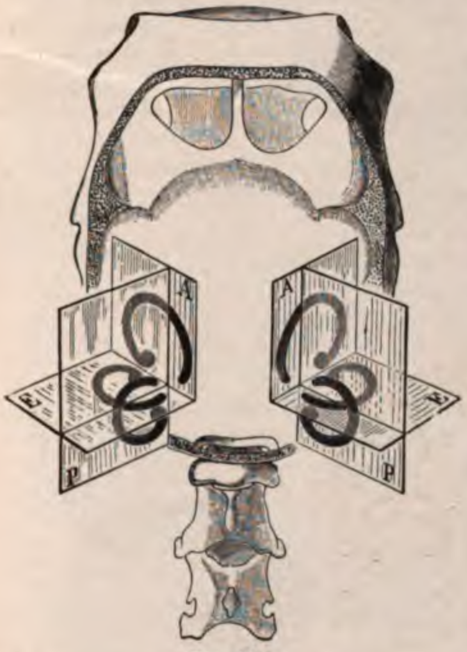

Fig. 185.

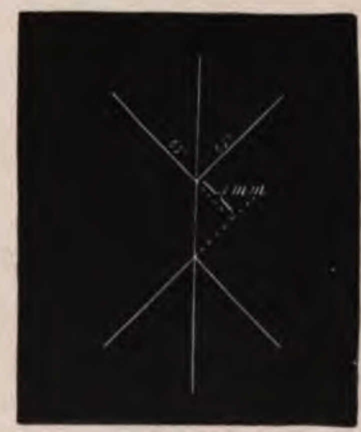

Fig. 186.

Fig. 185.—Schema showing the relations of the planes of the semicircular canals of the pigeon to each other, after J. R. Ewald. The open skull is seen from behind. The anterior canal lies in the plane *A*, the posterior in the plane *P*, and the external in the plane *E*.

Fig. 186.—Schema showing the distance of the planes of the anterior and posterior canals (prolonged) from each other.

These three (or two) otolith organs bear to each other the same spatial relations as the semicircular canals, the *macula utriculi* lying in the plane of the external canal, the *macula sacculi* in the plane of the anterior, and the *axis of the lagena* (where such can be made out) in the plane of the posterior canal.

It was long supposed that the semicircular canals and the ear sacs were called into play in the *perception of noises*—i. e., of sounds not produced by regular periodic vibrations—while the musical tones excited the nervous end organs of the cochlea. Conclusive proofs for this apportionment of the acoustic stimuli to two kinds of terminal auditory apparatus, however, were not forthcoming. Instead, it has been shown by numerous experiments that the semicircular canals and the sacs play a very important part in the mediation of our sensations of position, orientation, and the like.

B. EXPERIMENTAL SUPPRESSION OF THE SEMICIRCULAR CANALS

In 1828 Flourens published a paper on the phenomena which follow destruction of the semicircular canals of the pigeon. After transection of a canal he observed peculiar *pendulumlike movements* of the head in the plane of the canal transected. Thus, if the horizontal canal were the one operated on, the head was rotated incessantly to and fro in the horizontal plane. These movements ceased after a time; but if the corresponding canal of the other side were sectioned, the movements began again with still greater intensity. They came on suddenly, if the animal was disturbed in any way. The pigeons could no longer fly and could only take food with difficulty. The more extensive the destruction of the canals, the more intense were the disturbances produced, and the animals continued to exhibit such disturbances for years.

Goltz performed a great service for this line of investigation when he observed that the result of the operation can be described primarily as a disturbance in the ability of the animal to keep its body in *equilibrium*. He also laid stress on the idea that since this disturbance persists for several years after the operation, it must be regarded not as a symptom of irritation, but as a symptom of some *deficiency* caused by elimination of the semicircular canals. This, moreover, is confirmed by painting the canals with *cocaine*, exactly the same phenomena being produced as by section (Ch. Koenig, Gaglio). Goltz concluded that the semicircular canals constitute a peripheral sense organ, which supplements the visual and motor senses in

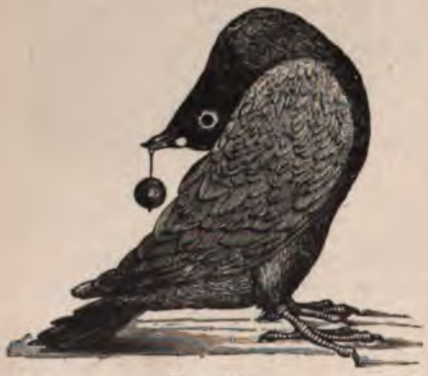
FIG. 187.

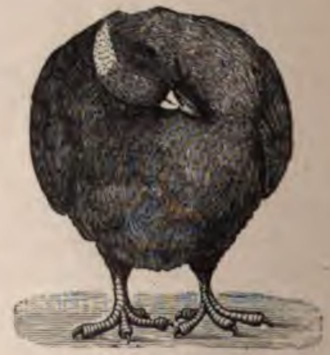
FIG. 188.

FIG. 187.—Pigeon with both membranous labyrinths removed, after J. R. Ewald.

FIG. 188.—Pigeon five days after removal of the right membranous labyrinth, after J. R. Ewald. The head is inclined toward the operated side.

the perception of the position of the head and thus indirectly in perceiving the position of the whole body.

After removal of the entire membranous labyrinth from *both sides* the pigeon on casual examination exhibits no particularly prominent symptoms for some months after the operation. But on closer investigation one finds that all the muscles are abnormally *atonic*, that the animals have a certain disinclination to move, that they cannot fly, and finally that their ability to recognize the position of their bodies is diminished.

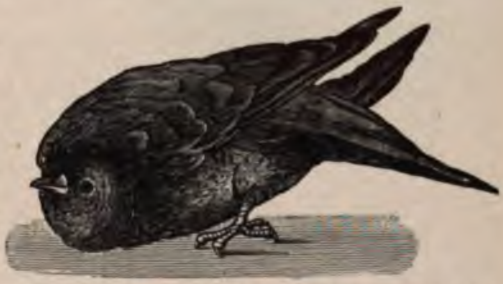

FIG. 189.—Pigeon twenty days after removal of the right membranous labyrinth, after J. R. Ewald. The head has been turned once around to the right.

The muscular weakness occasioned by the operation is demonstrated by the following experiment. A small lead ball weighing 20 g. is suspended on a thread and the thread is fastened by means of modeler's wax to the beak of a pigeon whose labyrinths have been removed. If the ball hangs in front, it draws the head far downward, but the relatively strong muscles of the back of the neck are able to lift it and to dangle it about. The head follows the pendulumlike movements of the ball apparently without concern but in reality quite powerlessly until at last in the course of its swinging the weight is thrown around over the back. Immediately this happens the head is held by the ball in the position shown in Fig. 187. The muscles which otherwise would lift the head from this position are too weak to do so now that the labyrinths are wanting.

The following experiment shows how the sensations of position are affected. A pigeon deprived of its labyrinth is blindfolded by drawing a leather cap over its head. Because of the muscular weakness the head falls down over the back and the muscular sensation fails to apprise the nerve centers of the fact. Since the visual impulses do not now compensate for this deficiency, the animal no longer has any correct notion of the attitude of its head, and will allow it to remain in this unnatural position.

After removal of the labyrinth on *one side only* the disturbances are less severe, so that the animals can still fly and can take food without difficulty. But they are not by any means normal, for the peculiar rotations of the head first described by Flourens, and which cease after bilateral extirpation, at times make their appearance.

During the first days following the operation the pigeon begins to incline its head toward the operated side. The turning increases more and more as time goes on, and finally may amount to complete rotation (Figs. 188 and 189). The explanation is, that by removing one labyrinth, say the right, the muscles which normally prevent the head from falling to the right are greatly weakened.

There is a decline in the *functional power of other muscles* after extirpation of one labyrinth. According to Ewald each labyrinth is connected by way of the central nervous system with all the voluntary muscles of the body, but more directly with those of the opposite side and in particular with those which move the head and vertebral column. Accordingly the muscles of either side would be roused to activity in any given case chiefly by the opposite labyrinth. In agreement with this is the fact that if one labyrinth be left intact and the other be suppressed, rigor appears sooner after the death of the animal on the side opposite the normal labyrinth.

In other species of animals extirpation of one labyrinth produces somewhat different results. In the rabbit rolling of the entire body around its longitudinal axis sets in soon after the operation. This is caused by extension of the legs on the opposite side, and by the consequent rotation of the animal toward the operated side until it comes to lie on its back. The animal tries to regain its feet, but as soon as it succeeds, begins once more to roll over. The legs of the operated side are entirely passive all the while. After bilateral extirpation in the dog, the animal exhibits a certain unsteadiness in his gait. When he jumps down from a table, he falls sprawling on the floor. Some difficulty in chewing and in swallowing may also be observed. All of which symptoms point to a reduction of muscular strength and of the ability to properly control the muscles.

The disturbances arising from bilateral extirpation of the labyrinths gradually disappear again. This occurs in all likelihood mainly because the animal gradually becomes accustomed to regulating his movements without the help of the afferent impulses from the semicircular canals.

The *cerebrum* appears to play the most important part in this regulation. With pigeons from which the cerebrum was removed, unilateral extirpation evoked the usual complex of symptoms, but some of them, especially the rotation of the head, were no longer compensated. After the symptoms accompanying bilateral extirpation in the dog had been improved as much as possible, J. R. Ewald removed the surface of the cortex from the motor zone of both sides. The dog exhibited disturbances of coördination of the profoundest kind. He could no longer jump or run or walk or even stand; in fact he could not lie on his belly. He lay rather on one side or the other, and despite his most vigorous efforts was unable to raise himself with his legs. The head, however, was used to more purpose. Gradually these disorders improved, but they immediately returned and in exactly the same fashion, as directly after the operation, when the animal was taken into a room which was suddenly darkened. The dog showed therefore that after exclusion of the impulses mediated through the labyrinths and through the so-called motor zone of the cortex, he had been thrown back upon his eyes for the regulation of his movements. Since now no such disturbances result from destruction of the cortex alone, even when the visual sensations also are excluded, it follows that after extirpation of the labyrinth the cerebral cortex takes upon itself the business of replacing the missing afferent impulses as far as possible. Then when the cerebral cortex also is destroyed, a compensation can once more be effected through the eyes, but this fails on exclusion of the visual sensations.

The disturbances which appear on suppression of the labyrinth are therefore, (1) a reduction of muscular strength, and (2) derangements in the coördination of movements, which to all appearances are due to the loss of afferent impulses.

C. ARTIFICIAL STIMULATION OF THE SEMICIRCULAR CANALS

Breuer (1874) made the first experiments of this kind and they were extended later by Ewald. In the following discussion we shall follow in the main Ewald's results.

The *anatomical structure* of the semicircular canals, as Breuer and Mach have pointed out, make it highly probable that the specific stimulus for the nervous end organs in the ampullæ consists of currents in the endolymph.

When a ring-shaped tube containing a fluid is rotated in the plane of its curvature the fluid remains for a time at rest on account of its inertia—i. e., a current is set up in the opposite direction relative to the walls of the tube, until the fluid has had time to acquire the speed of the tube. Such a current must result as often as a change in the speed or direction of rotation takes place. The same phenomena evidently must occur in the semicircular canals with every rotation of the head. But the effect in the different canals will depend upon their position with reference to the axis of rotation. Rotation about the vertical axis acts almost exclusively on the two external canals. If the head is turned to the right there arises in the external canal of the right side a current directed toward the end of the canal containing the ampulla, in that of the left side a current away from the ampulla. And thus there is in the different pairs of semicircular canals a current of a certain strength in a certain direction corresponding to every turn of the head. The sensory hairs of the maculæ are moved by these currents and in this way the corresponding nerve endings are excited.

These conclusions are capable of experimental proof by producing *movements of the endolymph* in a given direction. For this purpose Ewald opened a bony semicircular canal at two points. Into the opening farther from the ampulla he introduced a plug so that the movement of fluid in that direction was prevented. He adjusted to the other opening a small apparatus by means of which he could exert pressure on the naked membranous canal. Since the fluid could not move away from the ampulla, when pressure was applied a current of endolymph was naturally produced toward the ampulla. With every stimulus of pressure the animal (pigeon) invariably moved its head and eyes in the direction of the current and exactly in the plane of the canal stimulated. When the pressure was not released the animal brought its head back after a time to the starting point. If now the pressure was released and thus a current in the opposite direction was produced, the head and eyes were again turned, but this time in the opposite direction—i. e., always in the direction of the current of endolymph and in the plane of the canal stimulated.

Proof that the currents of endolymph give the normal stimulus to the semicircular canals is furnished also by *rotation experiments*. To prevent complications with the sense of sight the animal must be blindfolded. If a pigeon be placed in a rotation apparatus in such a way that it is rotated to the right about a vertical axis, it turns its head in the horizontal direction to the left, that is, in the same direction as the current produced by the inertia of the endolymph. When the head has been turned a certain distance to the left, it moves a certain distance to the right toward the median position, then is again rotated to the left, and so on. In this way the head swings incessantly to and fro and the eyes also take part in the movements. Now it is a probability supported by many facts that the first phase of the movement represents a reaction of the animal to the rotation; the second phase is produced, because after the head has been carried far enough from the median position the afferent impulses from the joints, muscles, etc., are strong enough to arouse the opposite sets of muscles.

When the two external canals are plugged up so as to prevent movements of the fluid, the reaction to rotation in the horizontal plane is almost entirely wanting. On the other hand, one can destroy any number of the anterior and posterior semicircular canals without changing the reaction.

The characteristic eye movements occur also when mammals are rotated; they are wanting after section of the eighth cranial nerve or of the semicircular canals.

From these facts we may conclude that the semicircular canals are influenced by movements of the head, and in all probability the immediate stimulus is caused by currents set up in the endolymph; this means that the sensory hairs of the corresponding crista acustica are put on the stretch and the appropriate end organs are consequently excited. These in their turn produce reflex responses by which the position of the head and of the eyes is regulated.

The movements of the eyes and of the head which have been seen to take place when the animal is rotated may appear after extirpation of the labyrinths when the eyes of the animal are open. At the beginning of rotation the animal experiences a displacement of the retinal picture, and seeks to resist that displacement by striving to hold the object steadily in view.

The subsequent motion of the head in the direction of the rotation is pure reflex, probably discharged by the excitation of the retina due to the displacement of the image or by impulses coming from the neck and eye muscles.

The effects of extirpation of the semicircular canals which have been summarized under B can be brought into line with these results without serious difficulty. Suppose a normal animal moves his head, say, to the right. The movement produces in both external semicircular canals currents in the endolymph in the opposite direction, and these in turn reflexly induce a rotation of the head in the direction of the current—i. e., in the direction reverse to the original rotation of the head. If the two external canals are now thrown out of function, either by being plugged or by being sectioned, the currents are not set up and consequently the muscular movements caused by them do not take place. But the head may swing to one side. If so, it will continue until the motor sensations from the joints, etc., discharge compensating movements. This mode of discharge, however, is not so finely graded, for the animal has lost the power of telling when the head has been returned to normal position; consequently it is difficult for the animal to regain its equilibrium after that has once been disturbed. When several canals are suppressed at the same time the swinging motions of the head become still more extensive.

The laxness of the muscles which has been observed affects most the muscles of greatest precision—e. g., the extrinsic muscles of the eyes—and is probably due to the absence of impulses normally roused by the labyrinth (Jensen).

D. THE OTOLITH SACS

It will be readily understood that a movement in a straight line will not produce any current in the semicircular canals, for the reason that the influence of inertia in the two halves of each canal will be found to be equal and in opposite directions. But, as Breuer has observed, it appears that the otolith apparatus may be stimulated under these circumstances. The impression which the otolith will make at any time will depend on the position with reference to the direction of gravity, of the surface between the otolith and the subjacent epithelium, and will vary, therefore, with the position of the head with reference to the line of gravity. On account of the varying position of the different maculæ, the impressions from the different otoliths for any given position of the head will also be different. Hence, every position of the head would be accompanied by a definite combination of impressions discharged by the otoliths, and hence the otolith sacs would constitute an organ for the perception of the position of the head with reference to a plumb line.

Again, if we suppose, as Breuer has sought to show, that each otolith has a definite "groove," so to speak, in which it may exert the pressure due to its inertia, we should have an arrangement by which translocation movements in any straight line could be perceived.

Several observations on fishes have been cited in support of this function of the otolith sacs, their purport being that when the sacs are injured or destroyed the orientation of the animal with reference to gravity is practically lost.

E. OBSERVATIONS ON MEN

The rotation experiments constitute a no less valuable means of studying the influence of the semicircular canals in man. When a man with normal ears is rotated about the vertical axis in an apparatus suitable for the purpose, the eyes are moved first slowly in the opposite direction, then quickly in the same direction as the rotation. This reaction appears to be perfectly constant in healthy individuals, but is often (fifty per cent of the cases [1]) wanting in the deaf and dumb (Kreidl).

Kreidl asserts furthermore that these same deaf-and-dumb persons who failed to give the eye reaction, did not suffer from dizziness when the rotation ceased, as the normal persons do, and similarly, we find in James the statement that out of 519 deaf-and-dumb persons only 199 suffered from dizziness as the result of rotation.

The explanation which Breuer has advanced with reference to the function of the otolith sacs in animals, namely, that they make the animal aware of its *position with reference to the line of gravity*, appears to apply also to man. Certain positions of the eyes are unquestionably dependent upon the position of the head with reference to the line of gravity. Thus, for example, in the blind the bending of the head forward is accompanied by an elevation of the plane of vision with reference to the head, and bending the head backward by a corresponding lowering of the plane of vision (Breuer). In persons with normal eyes these movements do not occur. But we meet with a wheel-like rotation of the eye about its axis when the head is bent to one side or the other. This is not caused by the nerves which convey muscular sensations, for the same rotation appears when the whole body is inclined one way or the other without bending the head or neck. When, for example, a person lying horizontally on his back turns his head to the right his eyes turn to the left, while with the same rotation of the head in a standing position no rotation of the eyes takes place. Such phenomena appear, therefore, to depend upon the changed position of the head with reference to the line of gravity. Since they are very different in character from those aroused from the semicircular canals, we should probably not go far astray in assuming that they are mediated by the otolith sacs, that is, that the latter furnish impressions which inform us of the direction of the line of gravity.

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[1] Mygind has ascertained that in Copenhagen about fifty-six per cent of the deaf and dumb have the semicircular canals affected.

These impressions do not figure prominently except under circumstances which exclude the ordinary visual, motor and tactual impressions, as for example in diving. It is said that many deaf-and-dumb persons lose all sense of direction when the body is submerged (James), also that such persons have great difficulty in standing on one leg, and when the eyes are closed find it quite impossible. We may suppose that in these persons the otolith sacs have undergone pathological changes.

The dizziness produced by sending an electric current transversely through the head is also thought to be due to stimulation of the labyrinth. When the current is closed the person feels as if the head and entire body were inclined toward the cathode; when it is opened one has the sensation of falling toward the anode.

From the observations and experiments here presented it appears quite probable that the labyrinth is a peripheral organ which reflexly regulates various finely graduated movements especially of the eyes and of the head, and in general is of considerable importance for the *tonus and functional capacity of the skeletal muscles.* If the conclusion is correct that conscious impressions as to the position of the head and orientation of the body are obtained from the labyrinth, it ought to be regarded also as an actual *sense organ* analogous to the organs of the motor sensations. That these impressions are usually indistinct says nothing against their occurrence, for superficially considered, the sensations aroused through the nerves of the tendons, joints and muscles, in spite of their demonstrably great importance, appear to us much less vividly than the sensations which proceed from sense organs stimulated by external agencies.

References.—*St. von Stein,* "Die Lehre von den Funktionen der einzelnen Teile des Ohrlabyrinthes," Jena, 1894.—*J. R. Ewald,* "Physiologische Untersuchungen über das Endorgan des Nervus octavus," Wiesbaden, 1892.—*J. Breuer, Wiener Sitzungsber.,* November, 1903.

CHAPTER XIX

TASTE AND SMELL

By means of the *sense of taste* we learn something of the solid and fluid substances taken into the mouth, and by means of the *sense of smell* something of the nature of the atmosphere entering the nasal cavities. The two senses very often work together, and many impressions which we ordinarily describe as sensations of taste, have, as a matter of fact, nothing whatever to do with the sense of taste, being mediated solely by the organs of smell.

§ 1. SENSATIONS OF TASTE

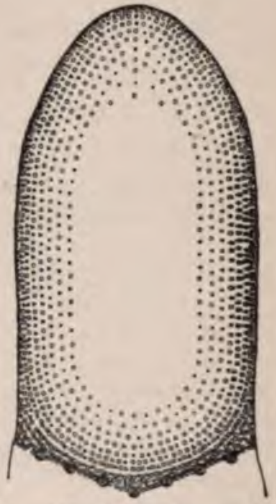

FIG. 190.—The taste zone on the upper surface of the tongue, after Hänig.

Ordinarily only the upper surface of the tongue is described as the *peripheral organ of taste.* But this appears to be incorrect, for according to different authors the under surface of the tip of the tongue, the soft and hard palate, the anterior pillars of the fauces, the tonsils, uvula, posterior wall of the pharynx, posterior side of the epiglottis and of the larynx, as well as the mucous membrane of the cheeks, mediate sensations of taste. However, this is true only of children; in adults the mucous membrane of the cheeks, the uvula, tonsils and middle of the tongue no longer react to sapid substances; in exceptional cases the anterior pillars of the fauces and the under surface of the tip of the tongue, both sides of the frenum, continue to be percipient. According to Hänig the central zone of the tongue which is not percipient is surrounded on all sides by a " taste girdle " within which the sensitiveness decreases more and more from the edge toward the middle line (cf. Fig. 190, where the sensitivity of the different portions is schematically represented by the number of black spots).

The end organs of the gustatory nerves are the taste buds or taste goblets discovered by Lovén and Schwalbe. They are ovoid bodies, 0.08 mm. long and 0.04 mm. thick, which lie imbedded in the epithelium of the mucous membrane. They consist in part of outer, sustentacular or tegumental cells and in part of inner taste cells which represent the true *neuroepithelium* connected in one way or another with the gustatory nerve fibers. In order to stimulate these taste cells the sapid substance must come into actual contact with them, and this is made possible by the presence of a small taste pore at the top of the taste bud, into which the attenuated ends of the taste cells project.

Because of the anatomical structure of the taste organ the entrance of the sapid substances in sufficient quantity to arouse gustatory sensations is rendered difficult, especially if the tongue is covered by a thick layer of mucus.

The taste buds are found chiefly in the circumvallate papillæ and in the sides of the foliate papillæ, but occur also in the fungiform papillæ, and are scattered here and there over the various parts of the mucous membrane of the mouth and throat endowed with the sense of taste.

The tongue possesses also nerves of touch, heat nerves, and cold nerves. What nerves supply gustatory fibers to the tongue can of course only be answered by observations on men in whom the afferent nerves from the tongue have been paralyzed in some way. It appears from such observations summarized by Cassirer that in by far the greater number of cases the gustatory **fibers for the posterior** part of the tongue traverse the glossopharyngeal, those for the **anterior** part the basal trigeminal nerve (Fig. 191). In certain cases it **appears, however,** that the glossopharyngeal represents the gustatory nerve **of the whole** tongue, while in others it may happen that all the gustatory **fibers traverse** the trigeminal.

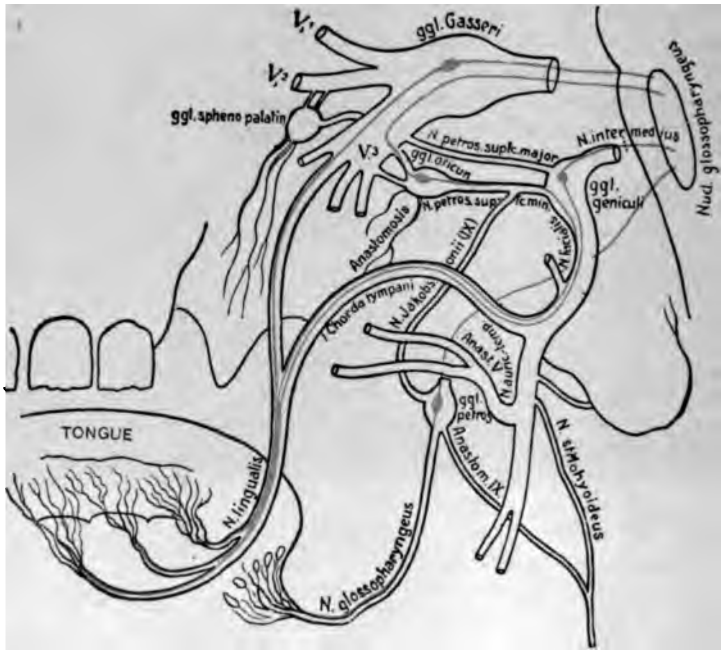

FIG. 191.—Course of the facial nerve and its communications with the **trigeminal and glossopharyngeal** nerves. The chief gustatory fibers are indicated in **red, after Leube.**

Only four qualitatively different kinds of sensation are mediated **by the** sense of taste; namely, *sweet, acid, bitter* and *salt*, to which ***alkaline* and** *metallic* are added by some authors.

These six qualities however cannot be regarded as pure taste **qualities, for** all of our gustatory impressions are accompanied by tactile sensations **(Kiesow).**

It is impossible to classify the gustatory impressions any further. For example, if we use solutions of HCl. HNO_3 H_2SO_4, acetic, tartaric and oxalic acids of such strength as to produce sensations of the same intensity, they all taste alike. The same is true of bitter substances like strychnin, quinin, morphin and picric acid, and of sweet substances such as milk sugar, grape sugar, cane sugar. On the base of the tongue we can distinguish all the taste qualities, but on the tip there are considerable differences in this respect in different individuals. v. Vintschgau recognizes four groups of individuals: (1) those who distinguish with the tip of the tongue all the four qualities; (2) those who distinguish sweet, salt and acid readily, but bitter less easily; (3) those who distinguish none of the qualities easily; (4) those who have no sense of taste at all on the tip of the tongue.

Moreover, the same substance placed on different parts of the tongue may have a different taste. Thus according to Howell and Castle brom-saccharin tastes bitter on the base of the tongue, but sweet on the tip. Shore found that a five-per-cent solution of $MgSO_4$ has a faintly sweetish taste on the tip of the tongue followed by an acid taste, an acid and bitter taste on the edge and a pure bitter taste on the base.

By means of cocaine the sensibility of the tongue to gustatory stimuli can be considerably reduced. But the effect is different for the different taste qualities. A five-per-cent solution of cocaine acts most markedly on the sense of bitter, then on sweet and acid, while it is entirely without effect on salt (Shore, Kiesow). The faintly toxic substance eucain has approximately the same effect. Gymnemic acid obtained from *Gymnema sylvestre* placed on the tongue in a sufficiently concentrated form obliterates every trace of sensitiveness for sweet (Edgeworth); it acts secondarily on bitter and to a much less degree on salt and acid (Shore, Kiesow).

It is very probable, from such observations as those just mentioned, that the different taste qualities are mediated by different nerves, just as in the case with the different qualities of the temperature sense. This inference has been directly confirmed by Ohrwall.

By means of a very fine brush he placed solutions of sugar, quinin and tartaric acid on different fungiform papillæ, and found that out of 125 such papillæ on the anterior part of the tongue 27 (21.6 per cent) did not react to either of these substances. Of the remaining 98, 12 reacted only to tartaric acid, 3 only to sugar, 12 only to tartaric acid and sugar, 7 only to quinin and tartaric acid, 4 only to sugar and quinin. No definite results were obtained with reference to the sensitivity of different papillæ for salt. Kiesow has reached similar conclusions.

Hoeber and Kiesow have discussed the significance of electrolytes as gustatory excitants, and have reached the conclusion that the specific sensations are aroused in part by ions. For example, the salty taste of KCl NaCl, $MgCl_2$, NaBr, NaI, Na_2SO_4 is caused by the electronegative ions (Cl, Br, etc.); the threshold stimulus is given by a concentration of 0.020–0.025 g. of the ion per liter; a sweet taste produced by a very weak solution is caused by the OH-ions, the threshold value of the stimulus being given by 0.006–0.009 g. ions per liter.

The acid taste produced by the anode of a constant current is probably due to electrolytic dissociation of the saliva.

§ 2. SENSATIONS OF SMELL

While the olfactory organ of man is particularly sensitive to certain odors, it in general is much less sensitive than that of many other mammals. The organ of smell is, in fact, much more important for the whole life of the lower animals, because it is mainly by this sense that they find and select their food. Among civilized men this sense plays but a small part for such purposes, although it is stated that some so-called wild people are possessed of a very highly developed sense of smell. Thus Humboldt relates that the Peruvian Indians can follow the trail by scent with as much accuracy as a hunting dog. Among civilized people the sense of smell serves to test the air inhaled or furnish information as to the nature of the food to be eaten. As a rule it is of no very great service even in this respect for the olfactory sense very soon becomes blunted for a certain odor and then gives us no indication of the presence of harmful substances in the air. This is notably true, for example, of those who live in close, poorly ventilated dwellings. The report made by the sense of smell as to the quality of the food is influenced largely by conventional customs, and these differ according to times and places. The olfactory sensations probably serve us most by arousing and promoting the desire for food.

It has long been known that only the uppermost part of the mucous membrane lining the nasal passages is provided with the *olfactory epithelium.* The investigations of v. Brunn have shown that the region actually supplied with olfactory nerves extends over only a relatively small part of the superior turbinated bone and the opposite face of the nasal septum. The epithelium here covers an area somewhat smaller than a ten-cent piece each side of the olfactory cleft, situated, therefore, in the roof of the nasal cavity as far removed as possible from the external nares.

Unless the act of inspiration is modified so as to carry the air directly to the upper part of the nose the air current never goes higher than the anterior lower edge of the superior turbinated bone (Franke) and consequently does not pass over the olfactory region. Since, however, we experience olfactory sensations in ordinary respiration and since we have convincing evidence that the normal excitation of the olfactory organ takes place by means of material particles in the air (see below) we must suppose that the odoriferous particles reach the olfactory cleft by diffusion.

Since the nose is always in open communication with the throat, odoriferous substances can of course always pass thence into the nose and so reach the olfactory cleft. This is what happens when we eat. While a morsel of food is being masticated vapors pass into the nasopharynx and are then carried upward into the olfactory region by the expired air. In swallowing the nasal cavity is closed off from the throat but immediately afterwards communication is reëstablished and the following expiration carries the vapor of substances moistening the wall of the pharynx into the nose. It is at this moment, but not so long as the fluid remains in the mouth, that one "tastes" the aroma or the bouquet of drinks.

It was thought for a long time that the olfactory organ is stimulated by *vibrations of the odorous substances,* and that the organ of smell was, therefore, analogous to the organ of hearing. The chief support of this view was that with certain strongly odorous substances no loss in weight could be detected with the balance, whereas, if it were true that the olfactory organ was excited by material particles set free from them there should be such a loss. But Berthollet demonstrated that material particles are given off from odorous substances. He placed a piece of camphor in a vacuum of a barometer; the mercury of the barometer gradually fell, thus showing that small particles of camphor were given off, that they collected in the empty space and exerted pressure on the mercury.

Another proof which we owe to Tyndall is the following: Radiant heat passes through an absolutely empty space without being absorbed; if, however, a gas is placed in the path of the heat rays, a greater or less amount of heat, according to the nature of the gas, is held back by it. Now Tyndall showed that an atmosphere which had been in contact with odorous substances and had taken up its vapor, absorbs radiant heat to a much greater extent than pure atmospheric air. Thus the vapor of patchouli absorbed thirty-two times as much as air, oil of rose thirty-six times, oil of anise three hundred and seventy-two times as much.

Odors are carried in a quiet atmosphere by diffusion. Of course air currents and the like also aid much in this distribution. The carrying power—i. e., the power of diffusion—varies with different odors.

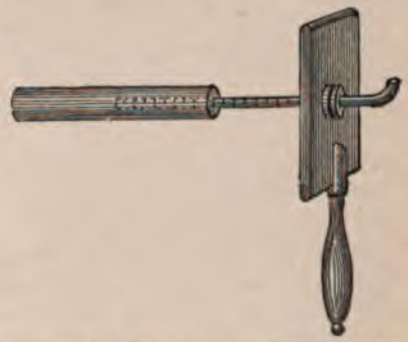

Fig. 192.—Olfactometer, after Zwaardemaker.

Johannes Müller and several other authors assumed that the particles of odoriferous substance were first dissolved in the mucus covering the olfactory region and then stimulated the olfactory epithelium. Since, however, very many odorous substances are very slightly, if at all, soluble in water, Zwaardemaker has put forward the hypothesis that stimulation takes place by *direct contact* of the gaseous molecules with the cilia of the olfactory cells. The fact that fishes—e. g., the dogfish—have a well-developed sense of smell speaks pretty definitely in favor of Müller's view.

Zwaardemaker has constructed a small apparatus, the olfactometer (Fig. 192), for the purpose of testing the acuteness of the sense of smell. The essential parts of this apparatus are a paper cylinder and a tube through which one may inhale. The cylinder, which can also be made of filter paper, is dipped in the scented fluid, and when its pores are filled with this, it is withdrawn, dried out and hastily blown through. The smelling tube, which fits exactly into the tubulure of the cylinder, is then inserted and the other end placed in the nasal opening. The small wooden shield serves to keep the odor out of the other nasal opening.

When air is inhaled through the tube from the cylinder impregnated with the odorous substance the number of odoriferous particles reaching the nose will vary inversely as the depth to which the smelling tube is inserted into the cylinder. By graduating the tube, one can thus make very rapid and very exact relative determinations as to the acuteness of the olfactory sense in different individuals.

The following data by Passy give some idea of the quantitative capacity of this sense in man. All the sources of error involved tend to make the results rather too high than too low:

	Mg. per liter of air.
Essence of orange	0.00005–0.001
Ether	0.0005–0.004
Camphor	0.005

The smallest value thus far published for the threshold value of the sense of smell is that of Fischer and Penzoldt. They observed that 0.01 mg. of mercaptan uniformly distributed through an air-tight room of 230 cubic meters capacity still gave a faint but distinct odor. This would be only 0.00000004 mg. of mercaptan per l. of air.

Attempts have often been made to find a *natural classification of the odors*, and it cannot be denied that recent efforts in this direction as well as the observations of Haycraft on the relation between the chemical constitution and the odor of various substances give promise that we shall some day have a real classification. For the present I shall only remark that many vaporous or gaseous substances act to a greater or less extent upon the organs of taste connected with the trigeminal nerve so that the resulting sensation is in large part at least the result of a gustatory excitation. This is true of all the so-called pungent substances like chlorin, iodin, bromin, nitric acid, acetic acid, ammonia, oil of mustard, etc. According to Zwaardemaker structures are found in the olfactory region which resemble the taste buds and which mediate the sweet odor of chloroform. According to Nagel we have to do in this case with a stimulation of gustatory nerves on the posterior side of the uvula.

Although we cannot yet erect a natural system of odors we can say definitely that different kinds of olfactory sensations, to a certain degree at least, are mediated by different nerves. Certain individuals who possess a well-developed sense of smell for some substances are unable to perceive the odor of others. For example, there are people who cannot smell vanilla and yet are sensitive enough to other odors. The same is true of the odor of violets. We must suppose that in these people certain nerve fibers or end organs are wanting.

The presence of *different olfactory nerves* is more definitely proved by the phenomena of fatigue of the olfactory organ. For example, Aronsohn has shown that when this organ becomes fatigued for one odor it still remains entirely functional for others. Again, when the sense of smell is temporarily lost as the result of injury to the olfactory organ, it is not recovered for all odorous qualities within the same time—e. g., in one case, for creosote three days, skatol and mercaptan four days, musk seventeen days, roast beef two months, etc. (Rollet).

REFERENCES.—*F. Kiesow*, "Geschmackssinn," "Wundt's Philosophische Studien," vols. x, xii, 1894, 1896.—*Hj. Öhrwall*, "Geschmackssinn," *Skandinavisches Arch. für Physiologie*, vol. ii, 1897.—*H. Zwaardemaker*, "Die Physiologie des Geruches," Leipzic, 1895.

CHAPTER XX

HEARING, VOICE AND SPEECH

FIRST SECTION

AUDITORY SENSATIONS

§ 1. STIMULI APPROPRIATE FOR THE ORGAN OF HEARING

The organ of hearing is stimulated by the vibrations of elastic bodies which we perceive as sound. Helmholtz, whose presentation of the subject[1] we shall follow here in the main, divides auditory sensations into two groups; namely, noises and musical tones.

A *musical tone* is produced by regular periodic movements of the sounding body, which are communicated by it to the air or some other elastic medium. By a regular periodic movement we mean a movement which is repeated at exactly the same interval of time, and always exactly in the same manner. The length of the interval from the beginning of one movement to the next repetition of it is called the wave length or the period.

As a rule, the vibrations are conveyed to the ear through the air. The particles of air must therefore execute *regular periodic vibrations*, moving to and fro within narrow limits so that the air is alternately condensed and rarefied (wave crest and wave trough). Sound is propagated in the form of concentric spherical waves, new particles of air in all directions from the sounding body being successively set in motion.

Three qualities of sound are to be distinguished: loudness, pitch and timbre.

A. LOUDNESS

The loudness of a sound depends upon the *amplitude of the vibrations*. The greater the excursions which, for example, a vibrating piano string describes, the louder is the sound at a given distance from its source. The greater the distance from the source, the weaker is the sound, the loudness being inversely as the square of the distance.

B. PITCH

Pitch is determined by the *vibration frequency*, or in other words by the number of vibrations per second, and is independent of the form of the vibration during the period. The more frequent the vibrations in a unit of time—i. e., the shorter the period—the higher is the tone.

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[1] "Lehre von den Tonempfindungen als physiologische Grundlage für die Theorie der Musik."

For an exposition of the fundamental facts of this subject it is very convenient to have a special apparatus, like the siren (Fig. 193), which permits an easy determination of the number of atmospheric vibrations producing different tones.

A is a thin disk of pasteboard or metal which is provided with holes in several concentric rows and at equal distances from each other in the same row. It can be set in rapid rotation by means of the string *f* which runs over the pulley *b*. By means of the tube *c* a blast of air of proper strength is directed toward one of the rows of holes. Each hole therefore as it passes the mouth of the tube lets out a single puff of air and thus when the disk is rotated rapidly enough a tone is produced whose pitch depends upon the number of holes blown through in a second of time. This number can be found by counting the rotations.

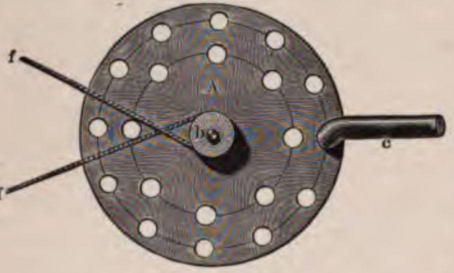


FIG. 193.—Seebeck's siren.

Now experiment has shown that pitch is entirely independent of the size of the holes or the strength of the blast and thus it is proved that pitch depends only on the number of vibrations.

The nearer the row of holes to the center of the disk—i. e., the smaller the number blown through in a single rotation—the lower will be the tone, the rate of rotation remaining the same. If one row with 8 and another with 16 be employed the tone produced by the latter is the octave of that produced by the former—i. e., the tone which constitutes the higher octave of the other contains within a given time exactly twice as many vibrations as the other, and the ratio of the two is as 1 : 2.

In the same way the following ratios have been found to obtain between the number of vibrations of the different tones used in music: 1 : 2 = octave; 2 : 3 = a fifth; 3 : 4 = a fourth; 4 : 5 = major third; 5 : 6 = minor third; 5 : 8 = minor sixth; 3 : 5 = major sixth. These are all consonant intervals —i. e., in the octave every second vibration of the upper note begins at the same time with one of the lower; in the fifth, every third; in the fourth, every fourth, etc.

There is an upper and a lower limit to the frequency of periodic vibrations capable of exciting the auditory organ.

The smallest number per second which can be heard by the human ear is given by Preyer as 15–24, by Helmholtz as 28, by Bezold using highly improved experimental methods as 11; but sounds only begin to acquire a definite musical pitch at about 40 vibrations per second. The highest number which can be heard as a distinct sound according to Edelmann is in the neighborhood of 50,000. The whole range of perceptible sounds (11–50,000) amounts therefore in the most favorable case to over 12 octaves. In music only about 7 octaves (40–4,700 vibrations) are used.

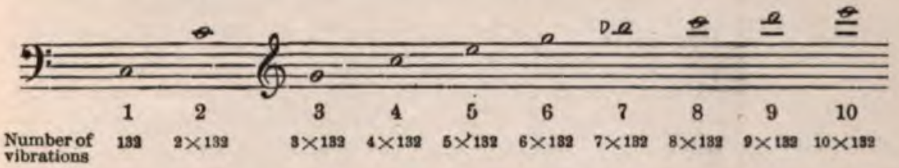
C. TIMBRE

If the same tone be struck successively on different instruments, as the violin, piano, clarinet, flute, etc., even a musically untrained ear can readily distinguish the instruments. This property of a musical tone which differs with the instrument producing it is described as the *timbre* or *quality*. It is this property also by which we distinguish human voices.

Inasmuch as the cause of timbre cannot lie in the frequency nor the amplitude of the vibrations, it must be referred to *dissimilarities in their form*. To a certain extent also it is due to the way in which the tone is struck.

How is this difference in form of the vibration to be explained? When a piano string is set in vibration the pitch of the tone produced depends upon two things: the *length* of the part vibrating, and the *tension* of the string. The tension remaining the same, the longer the vibrating part the deeper the pitch. If the operator touch the middle of a string lightly with his finger and then cause it to vibrate, each half will vibrate independently and so twice as many vibrations per second are made as by the whole string. The tone produced is therefore the octave of the tone given by the whole string. In the same way a string can be caused to vibrate in thirds and fourths, etc., and the number of vibrations of the corresponding tone will then be three, four, etc., times as high as that of the whole string.

Now whenever the string vibrates as a whole, it divides itself spontaneously into two, three, four, five, etc., vibrating parts. Hence, it gives in addition to its fundamental tone other tones whose vibration frequencies are two, three, etc., times as great as the fundamental, all of them fused into the peculiar sound of that particular string. The tones produced by the partial vibrations of the string are called the overtones or partial tones, and when the vibration frequency of the overtones is a multiple of that of the fundamental, they are called harmonious overtones. The harmonious overtones for *c* are given in the following example:



What has been said of the piano string is true for musical instruments in general, inclusive of the human voice. But there are sounds which are fairly free of overtones and so consist of a simple tone only—as, e. g., the proper sound of a tuning fork. Such tones are unusually soft, and free from sharpness or roughness. Comparing the timbre of a simple tone with that of a compound tone, including its lower harmonious overtones, the latter is found to be fuller sounding, more metallic and brighter than the simple tone.

Since by far the greater number of tones are compound it is evident that any variation in the number or intensity of the overtones will produce some difference in the character of the tone; hence we may point to differences in the accompanying overtones as very probably the cause of difference in timbre.

There remains for us yet to consider how it is possible for the ear to perceive the differences in the form of vibration caused by the overtones.

The effect of overtones in altering the form of vibration may be represented diagrammatically as in Fig. 194. *a' a'* is the base line of reference, the dotted lines *a*, *b*, and *c* represent the vibrations of a fundamental tone (*a*) and its first two overtones; the solid line *d* is the resulting vibration produced by interference of the three. It is evident that notwithstanding the change in form of the vibration the period of the fundamental tone remains unchanged.

But if these partial tones are not to be regarded as mere mathematical fictions, if they have a real existence, they should produce some mechanical effect which is recognizable. Such an effect we find in the phenomenon of ***sympathetic vibration*** (resonance), occurring in all bodies which, once they are given the impetus, run through a series of different vibrations before they come to rest. The simplest example of this is witnessed when a certain note is sung into a piano. The same note is given back by the piano, its intensity bearing a direct relation to the exactness with which the note of a particular string is struck by the voice. Sympathetic vibrations between bodies producing compound tones can be aroused even in case the vibration frequency is not exactly reproduced, and this takes place more readily the smaller the mass of the sympathetic body (e. g., a catgut string responds more readily than a wire string of the same diameter). But it is much more difficult to induce sympathetic vibrations from a body which gives no overtones—e. g., from a tuning-fork—because it will respond only to its own particular form of vibration.

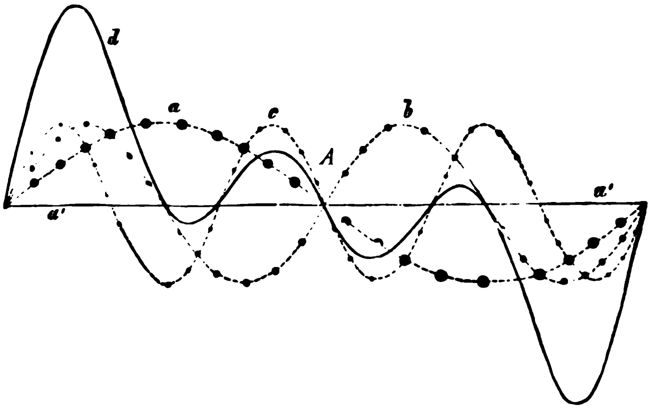


Fig. 194.—Schema illustrating the relation of overtones to their fundamental tone, after Hensen.

It has been shown that a membrane adapted to a certain tone also exhibits the phenomenon of sympathetic vibrations, if a lower tone, which contains the tone of the membrane among its overtones, is sounded. The tympanic membrane of the ear is not adapted to any one tone—i. e., has no fundamental tone—hence does not select any single tone by resonance.

The actual presence of overtones can be demonstrated still more clearly by the use of the Helmholtz resonators. These may have different forms. The one shown in Fig. 195 has the form of a hollow sphere, one opening (*a*) of which ends abruptly, while the other (*b*) is drawn out funnellike and so shaped as to fit into the ear. The air of such a resonator in conjunction with that of the auditory passage and the eardrum forms an elastic system, which intensifies the fundamental tone of the sphere. Of course, one can have a whole series of resonators adapted to the different tones. If now a certain resonator be placed to the ear and the attention is directed to a sound or series of sounds in which the particular tone of that resonator occurs, this tone will be intensified to so great an extent that it can readily be heard above the others.

These and other observations which we cannot go into here make it perfectly certain that the different overtones actually exist in compound tones.

The following experiment shows directly that the *ear also can receive these overtones* and is therefore sensitive to each and every simple vibration of this kind. If the tone *g* of the first octave be struck on the piano and immediately afterwards the tone *c* of which *g* is the second overtone and the attention be directed steadily to *g*, one can hear it in the tone *c*, after the *g* string has ceased vibrating. In the same way one can convince himself that *e* of the second octave is one of the overtones of *c*. Often the overtones become clearer as the string ceases to vibrate, for it appears that they die out more slowly than the fundamental tone.

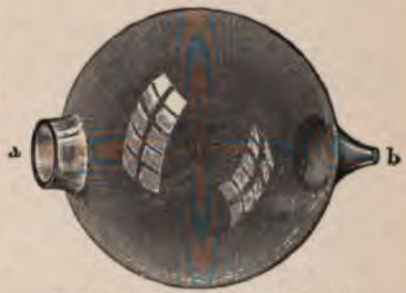


FIG. 195.—Resonator of Helmholtz.

The ability of the ear to *analyze sounds* into their constituents is attested by our every-day experiences that we can easily distinguish the individual tones of an organ though only a person musically trained can name them.

The facts which make it possible for the ear to analyze sound may be summarized briefly as follows. *Every movement of the atmosphere which represents a compound of tones can be resolved into a number of simple pendulumlike vibrations, and for each such vibration there is a tone perceptible to the ear whose pitch is determined by the vibration frequency of the atmospheric movement* (Ohm's law).

How does the ear accomplish this analysis? Since the endings of the auditory nerve are found in the internal ear, it is plain that analysis of sound must take place there, also that sounds must be transmitted thither without any considerable change. These phenomena will occupy us in the pages immediately following.

§ 2. TRANSMISSION OF SOUND IN THE EAR

The external and middle ear together constitute merely an apparatus for the *transmission* of sound, and careful investigation of auditory sensations has shown that this apparatus is able to transmit sound waves to the internal ear without any considerable modification.

A. THE EXTERNAL EAR

Since, owing to the feeble development of the ear muscles, the human *pinna* cannot be turned in different directions, it is of but slight service in the collection of sound waves. It has been shown also that the reflection of sound waves by the pinna is of no importance (Harless, Mach).

The *external auditory meatus* ought probably to be described as a means of protection for the eardrum. The indirect course of the canal itself favors this view, since in order to see the drum the pinna must be drawn considerably upward and backward. Besides, this canal is provided with sensitive hairs which together with the disagreeable odor of the earwax secreted in the canal serve to prevent the entrance of insects. The passage also protects the middle and internal ear from variations of temperature.

Like every hollow space of the kind the external auditory meatus has its own resonance tone, situated between c^{IV} and a^{IV}[1] (Helmholtz, Hensen). If this tone be contained in a sound, naturally it will be intensified above other tones by the sympathetic vibration of the air in the canal, but owing to its high position in the scale its resonance is of no great consequence from a practical standpoint.

A tuning fork allowed to die out until the vibrations are just imperceptible when it is held close to the ear, can be heard again if the handle be placed between the teeth. In this case the sound is conducted in part directly through the bones of the head to the internal ear and in part is transmitted from the bones to the eardrum and propagated thence as usual through the auditory ossicles.

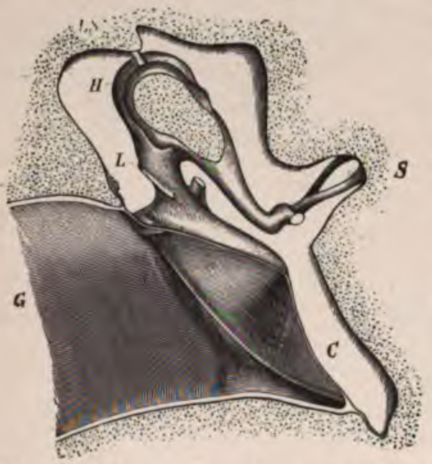


FIG. 196.—Transverse section through the left auditory canal and tympanic membrane of man, enlarged four times, after Hensen. The section is taken just behind the handle of the hammer in a plane parallel to the handle. *G*, external auditory meatus; *C*, tympanic cavity; *S*, the stapes; *H*, the hammer; a ledge projects at *L*, to which the ligaments are attached. Between the long process of the anvil and the handle of the hammer the tendon of the tensor tympani may be seen; *LS*, ligamentum superior.

B. THE MIDDLE EAR

1. *Vibrations of the Eardrum.*—The tympanic membrane or eardrum is a fibrous membrane 0.1 mm. in thickness, formed mainly of external radial and internal circular fibers. It is obliquely placed across the internal end of the external auditory meatus and is drawn inward at its middle by the long process of the malleus which is inserted into its tissue along one of its radii. In this way the membrane is given the form of a shallow, irregular funnel with an aperture of about 125° (Fig. 196).

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[1] The small Roman numerals designate octaves.

The membrane is set in vibration by the oscillations of the atmosphere and is so arranged that it does not favor any particular tone.

Fick has worked out the following conception of the mechanics of the drum. The radii from the tip of the long process of the malleus to the periphery of the drum being of different lengths, the different sectors of the drum may be looked upon as to a certain extent independent of each other. If they were entirely independent strands, each would vibrate in response to its own particular tone. Being joined together into a membrane they do not thus select individual tones, although separate parts can be thrown into action without moving distant parts very much. Consequently, because of the summation of successive vibrations, regular periodic movements are more favorably received by the drum than single vibrations. And yet vibrations of any form or frequency are faithfully transmitted to the handle of the malleus, for among the sectors and segments of the membrane there are always some which are suited to the component vibrations. Since, however, the malleus is a rigid body and can only vibrate as a whole, all the components will be represented in the form of its movements.

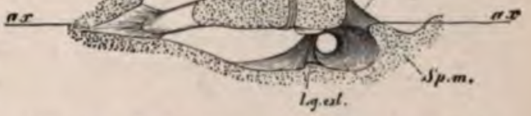

FIG. 197.—Nearly horizontal section through the tympanic cavity, *CT*, of the right ear, enlarged four times, after Hensen. The section is taken just above the notch of Rivinus and vertical to the plane of Fig. 196. *H*, medial edge of the head of the hammer. *A*. anvil. The ligamentum anterius, *Lig. a.*, is seen springing from the larger process, *Sp. m*, of the wall of the tympanic cavity and passing to the hammer where it becomes continuous with the ligamentum laterale. *Ll* of the anvil-hammer joint. The ligamentum externum, *Lig. ext.* springs the notch of Rivinus and passes to the hammer.

The peculiar form of the tympanic membrane is of special significance in another respect also; the sound waves converging toward the middle point are damped—i. e., diminished—in amplitude, but are increased in intensity. This aids greatly in the transmission of vibrations to the perilymph (Helmholtz).

2. *The Auditory Ossicles.*—For the anatomical details of the auditory ossicles the reader is referred to text-books of anatomy. We give here briefly only the facts with reference to their mode of attachments, as made out by Hensen and Schwalbe, which are of most importance for an understanding of their physiological purpose (Figs. 196 and 197).

The *malleus*, or hammer, is attached to the wall of the tympanic cavity by three ligaments (Fig. 197). The first of these, the anterior, passes from the *processus longus* and around its base partly to the larger spine of the tympanum (*Sp. m.*), partly through the Glaserian fissure to the angular spine of the sphenoid bond. The second or external ligament (*Lig. ext.*) is a short tense band which springs from the whole posterior half of the notch of Rivinus as far as the smaller spine of the tympanum opposite the hammer, and from this relatively long line of insertion its fibers converge to the *crista mallei*. The third or superior ligament (Fig. 196, *LS*) limits the movability of the ossicles downward.

The tip of the short leg of the *incus* is fixed by means of a strong ligament (ligamentum incudis posterius) to the opposite wall of the tympanic cavity.

When the tympanic membrane moves in and out in response to the atmospheric vibrations the handle of the hammer naturally moves with it; but the head of the hammer moves in the opposite direction. Too great an excursion of the handle outward is prevented by the external ligament.

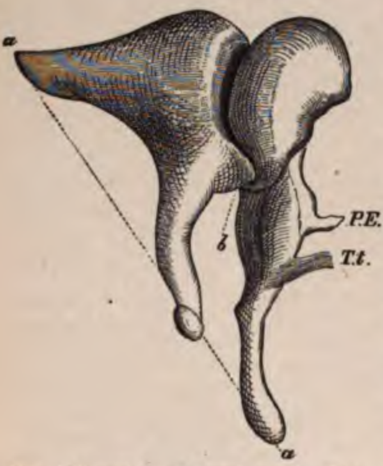

Fig. 198.—Hammer and anvil, after Helmholtz. *PE*, processus Folianus; *Tt*, tensor tympani; *b*, ratchet tooth of the anvil.

The *incus* articulates with the head of the malleus by means of a peculiar saddle-shaped joint, the physiological significance of which has been pointed out by Helmholtz. This joint is provided with ratchet teeth, which, as will be evident from inspection of Fig. 198, engage each other in such a way that the incus is carried along with every movement of the manubrium inward, while they are disengaged when the manubrium moves outward. In this way the danger of tearing the stapes from its fastening in the foramen ovalis when the tympanic membrane is for any reason pushed outward, is diminished. Helmholtz estimates that the hammer can be rotated five degrees outward without carrying the anvil with it.

If we imagine the hammer and anvil locked together by their ratchet teeth so that the two move inward as one solid body, the system formed by the two ossicles can be regarded as a one-armed lever, the fulcrum of which lies where the apex of the short process of the anvil is supported against the wall of the tympanic cavity. The tip of the manubrium constitutes the point where the power is applied, the apex of the long process of the anvil the point where the load —i. e., the stapes—is acted upon. These three points lie almost exactly in a straight line, the joint between the stapes and anvil lying only a little inside the line joining the other two. The lever *a a* (Fig. 198) is about 9.5 mm. long, the short arm between the two apices of the anvil being about 6.3 mm.—i. e., just two-thirds of the long arm.

It follows that when the hammer and anvil are firmly engaged, the excursion of the incus-stapes joint is only two-thirds that of the apex of the manubrium, but the pressure which the stapes exerts on the oval window is one and one-half times as great as that which acts upon the apex of the manubrium (Helmholtz).

The top of the *stapes* is attached by a strong ligament to the long process of the incus, and its base is fastened into the fenestra ovalis by means of a thin membrane. The stapes must accompany all the movements of the long process of the incus, so that when the tympanic membrane moves inward, the base of the stapes is pressed into the labyrinth. At the same time there takes place a slight rotation of the stapes around the long axis of its base. A limit is set to the movement of the base inward by the resistance of the membrane holding it in the oval window.

Politzer attached threads to the malleus and incus and recorded their movements on a revolving drum. In this way he was able to show by direct experiment what is supported also by theoretical considerations, namely, that sound is transmitted from the tympanic membrane to the labyrinth by ***molar*** movements of the auditory ossicles and not by ***molecular*** movements.

The *round window* is closed by a thin membrane bathed on the inside by the perilymph. The perilymph being incompressible, this membrane in all likelihood constitutes an arrangement by which the movement of the stapes inward can be compensated by an equal movement outward. The endolymph has a similar protective device in the ductus endolymphaticus, which is connected on the one hand with the utricle and saccule and by these with the scala media of the cochlea, and on the other passes through the petrous bone and terminates on its posterior surface in a little vesicle underneath the dura mater.

The round window might also serve for the purpose of conveying vibrations to the perilymph, and this in fact has been observed when the oval window was rigidly closed.

By means of a capillary manometer introduced into the superior semicircular canal, Bezold was able to determine the extent of the movements described by the conducting apparatus of the human ear with the tympanic cavity open. The maximum movement of the *manubrium* caused by variations of atmospheric pressure in the external auditory canal was about 0.76 mm. from one extreme to the other, one-third of this being the movement inward and two-thirds the movement outward.

As Bezold remarks, this difference between the movement inward and outward is difficult to harmonize with an exact transmission of sound waves, and probably would not occur under normal circumstances. As a matter of fact we have in the *internal muscles of the ear* a device which in life might correct this lack of coördination observed after death.

These are the *tensor tympani* and the *stapedius* muscles, the former innervated in the main by the trigeminal nerve, the latter by the facial. The tensor tympani draws the manubrium inward and thereby presses the stapes farther into the labyrinth. It serves thus to keep the chain of ossicles " keyed up." Section of its tendon permits a moderate magnification of the movement of the whole chain and the increase is almost exclusively in the outward movement (Bezold).

Experiments on dogs have shown that the tensor tympani contracts reflexly to acoustic stimuli (Hensen, Hammerschlag *et al.*) acting through subcortical centers not higher than the posterior corpora quadrigemina (Ostmann).

Hensen looks upon the tensor tympani as an apparatus for accommodating the ear in listening to faint sounds, and cites as evidence the fact that a weak sound becomes stronger for the moment when strong motor impulses are sent out, say to the muscles of the face or limbs. The explanation would be that impulses are at the same time sent to the tensor tympani muscle.

Ostmann would ascribe this function to the stapedius.

3. *The Tympanic Cavity and Eustachian Tube.*—In order that the middle ear may fulfill its purpose of transmitting the vibrations of the atmosphere

to the labyrinth to the best advantage, it is necessary that all extraneous vibrations be excluded as far as possible. Moreover, the tympanic cavity ought, if possible at all, to have no tone of its own, and finally no difference of atmospheric pressure, at least no permanent difference, ought to obtain between the tympanic cavity and the outside air.

These requirements are sufficiently fulfilled, one can readily see, by the structure of the *tympanic cavity*, this being at once rather small and very irregular in shape, so that resonance to special tones is prevented.

The pressure inside the tympanic cavity is regulated through the ***Eustachian tube*** communicating with the throat. Normally this tube is rather tightly closed, but it is often opened—as, e. g., in swallowing. Since it is in this way that the pressure inside and outside the tympanic cavity is equalized, it is well for a person inclosed within a pneumatic cabinet, where the air pressure is considerably increased, to swallow frequently. The tube is opened also in strong inspiration and in phonation, although to a less extent than in swallowing.

The Eustachian tube is lined with a ciliated epithelium which probably serves to drive the mucus, etc., toward the throat.

§ 3. EXCITATION OF THE AUDITORY NERVE

The vibrations of the stapes are transmitted to the perilymph, and these in turn set the endolymph in vibration.

A. THE RESONATORS IN THE COCHLEA

We have already remarked that the analysis of sound leads us to assume that the different perceptible sounds have their appropriate ***resonators*** in the ear. But it is possible also to imagine that the fibers of the auditory nerve themselves are thrown by the endolymph into vibrations which agree exactly with those of the conducting apparatus. Against this hypothesis, however, several objections may be urged, chief of which is that we have nowhere else in physiology any analogous production in a nerve itself of 40,000 or 50,000 molecular vibrations per second. Besides, there are some observations which appear to speak directly in favor of the resonance theory. For example, Bezold has found by means of an instrument which enabled him to vary the number of vibrations per second from that of the lowest sound to that of the highest, without any omissions, that for different individuals there are gaps of greater or less size in the series of perceptible tones. Some show defects both in the upper and the lower ends of the series, others only in the lower, and still others only in the upper end. Gaps of varying extent occur also at different places along the course of the scale. All of them can be explained by supposing that the corresponding resonators are wanting.

That the fibers of the auditory nerve are not set in vibration directly by the vibrations of the endolymph is indicated by the following considerations with reference to fatigue of the ear:

If the vibrations of a tuning fork in a distant room be transmitted by means of two telephones to the two ears, the tone will appear to be located exactly in the mid line of the head. If it be transmitted to only one ear for a time, and then the two telephones be used again, the tone appears now to be on the side of the ear which was resting. If in this way the one ear be fatigued for a tone say of 360 vibrations per second, and immediately afterwards one of 365 vibrations be transmitted to both ears, the one fatigued for 360 vibrations will show no trace of fatigue for the new tone. It is difficult to see how the nerve fibers could be excited directly by one of these tones and not by the other. The difficulty disappears by supposing that each has a resonator which is not affected by the other.

We can think of the analysis of tones, therefore, as follows: In the internal ear there are a large number of *resonators* adapted for different tones, which are called into play if the appropriate vibrations are transmitted to the endolymph. Each of these resonators in some way affects a nerve fiber. The excitation thus aroused is transmitted to the brain and there, according to the nerve fiber which brings it, gives rise to a perception of one tone or another.

In order to test the plausibility of this hypothesis it is necessary to inquire whether the structures which might be regarded as resonators are present in sufficient number to account for the analytical powers of the ear.

Only exceptionally does one meet with a man who cannot tell definitely which of two successive tones is the higher, provided that the interval between them really is great enough. In musically educated individuals this ability is very great. According to Preyer trained persons can recognize a difference of 0.3–0.5 vibrations per second within the range from a^{I} to c^{II}; above and below this range the ability is much less—e. g., with c^{V} errors of as much as one hundred and more vibrations may occur.

According to Helmholtz's calculations some 4,200 resonators—i. e., 600 per octave—would be sufficient to account for the best possible discernment of fractions of a half tone. Besides this, 300 resonators would be enough for the tones not used in music—i. e., 4,500 in all.

We have seen that the semicircular canals and the otolith sacs probably have no acoustic functions, or that at most they take part only in the perception of noises (cf. page 475). The whole structure of the nerve endings in the cochlea, on the other hand, favors the view that the peripheral organ for the analysis of sound is to be sought here.

On the basilar membrane (Fig. 199, *mb*) we find the organ of Corti. This contains a very large number of rodlike structures, the *pillars of Corti* (*ic* and *äc*), standing side by side throughout the whole length of the cochlea and bound together by means of a joint at the top into pairs.

These pillars are surrounded outside and inside by peculiar epithelial cells, some of which, the *outer* (*äh*) *and inner* (*ih*) *hair cells*, bear hairlike processes ending freely in the endolymph. These cells are in connection with the endings of the auditory nerve. The *basilar membrane* is of varying width at different parts of the cochlea and contains fibers which are stretched transversely to the cochlear canal. These are imbedded in a transparent matrix.

The required resonators must be found among these structures and their number is quite sufficient for the purpose; for, according to Retzius, the cochlea of man contains 5,600 inner pillar cells, 3,850 outer pillar cells, 3,500 inner hair cells, 12,000 outer hair cells (in four rows), and 24,000 fibers in the basilar membrane.

We can only conjecture which of these structures are the true resonators. Originally, Helmholtz ascribed this function to the pillars of Corti; later, however, he gave up this view because it was found that birds and reptiles have no such pillars in their auditory organ. After Hensen had established the fact that the basilar membrane varies in width in different parts of the cochlea,

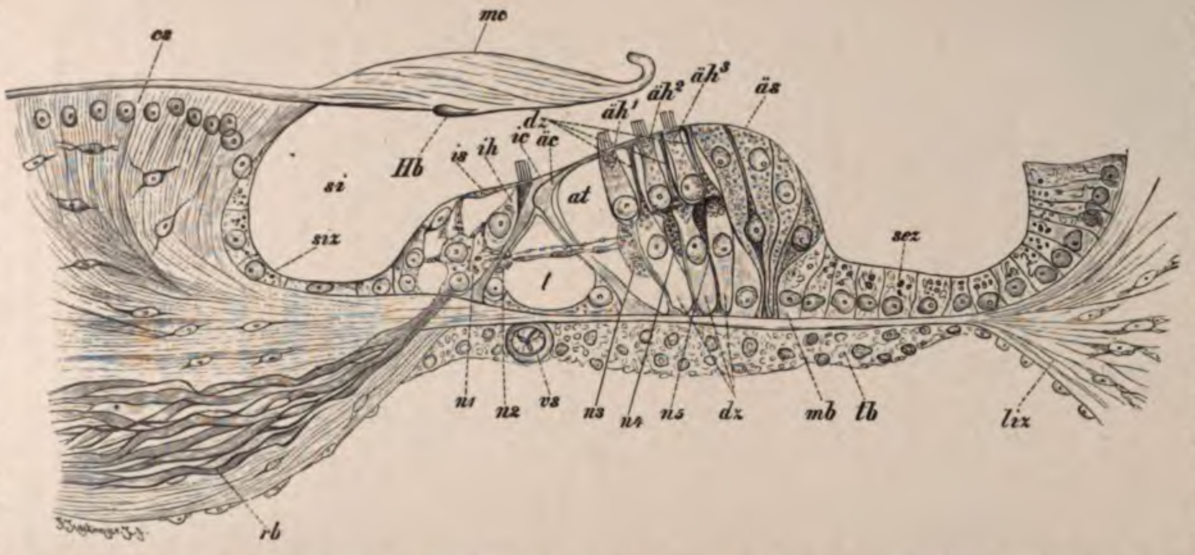

FIG. 199.—Organ of Corti of the human ear, after G. Retzius. *mc*, membrana tectoria; *rb*, nerve fibers of the cochlear nerve; *siz*, epithelium of the sulcus spiralis internus; *mb*, basilar membrane; *liz*, ligamentum spirale; *tb*, investing layer in the scala tympani; *vs*, spiral vessel; *n1*, ending of inner spiral nerve fibers; n^2, ending of fibers within the tunnel of Corti; *n3*, *n4*, *n5*, endings of outer spiral nerve fibers; *is*, inner sustentacular cells; *ih*, inner hair cells; *ic*, inner pillar cells; *äc*, outer pillar cells; *t*, tunnel of Corti; *äh1*, *äh2*, *àh3*, outer hair cells; *dz*, Deiter's cells; *äs*, Hensen's sustentacular cells; *sez*, epithelium of the sulcus spiralis externus.

Helmholtz sought the resonators in the transverse strands of this structure. In a membrane of this kind where the longitudinal tension is small as compared with the transverse tension, the radial fibers act like a system of separate strings. The membrane connecting them serves only to give the pressure of the fluid a purchase on the strings and each one will therefore vibrate independently of the others.

Finally, the hair cells might serve as resonators. In short, although we cannot settle definitely on a choice between these various elements, it must be evident that there is no lack of structures suitable for such a function.

B. OBJECTIONS TO THE RESONANCE THEORY

The resonance theory of Helmholtz fits in remarkably well with the facts mentioned thus far. But there are some circumstances under which the theory cannot be applied so readily, and these circumstances must not be passed over in silence.

1. *Beats.*—When two tones of different vibration frequencies are sounded at the same time, if the difference between them is not too great, the vibrations of the two will interfere with each other, producing what are called beats. Thus if the difference in the number of vibrations be only one per second, and if the two tones be struck at the same instant, the air waves of the deeper tone will gradually fall behind those of the higher until at the end of a half second the summit of one wave will coincide with the valley of the other; after another half second the two summits will coincide, and so on. And in general if n represent the number of vibrations of a tone per second, and $n+1$ that of another, then the loudness of the tone will be increased every second and be diminished every half second. The number of beats per second therefore will always be equal to the difference in the number of vibrations per second between the two tones.

Now if each tone has only one independent resonator in the cochlea, it is difficult to see how it would be possible for two tones to influence each other in this way. There is, however, very good reason for believing that each tone excites several neighboring resonators, and the difficulty offered by beats for the resonance theory is readily disposed of by this supposition. For two tones lying close together we suppose must influence several resonators in common; then since the objective strength of the tone varies incessantly because of the interference, the sympathetic vibrations of the resonators common to the two must likewise vary in strength, and hence the subjective sensation must present similar variations. Other phenomena connected with beats can be explained from the same viewpoint.

2. *Combination Tones.*—When two tones not too close together in the scale are sounded at the same time, one may hear, as was first pointed out by Sorge (1740) and Tartini, a true tone, the vibration frequency of which is equal to the difference in the number of vibrations per second between the two. For example, striking a fundamental and its fifth at the same time (ratio 2 : 3), one hears the lower duodecime of the fundamental. The first difference tone then forms a second difference tone with the first primary tone. Under certain circumstances a tone may also be perceived which represents the sum of the vibration frequencies of the two primary tones (Helmholtz). These *difference tones* and *summation tones* are included under the term combination tones.

Lagrange and Young regarded the difference tones as a kind of beats and explained them on the assumption of subjective interference. If this were shown to be true, it would constitute an absolute refutation of the resonance theory, for these particular tones would then have no objective existence and so could not, as the theory demands, excite resonators in the ear. The summation tones would constitute still greater difficulty for the theory.

Helmholtz, however, found an explanation for these tones by supposing that either the tympanic membrane or the incus-malleus joint, or both, are not uniformly elastic, and that the combination really takes place therefore in the conductors of the ear. Several authors do not find this explanation wholly satisfactory and, because of this and other difficulties which cannot be entered into here, have given up the resonance theory altogether and adopted other views. When all has been said, however, it is the opinion of the author that the resonance theory is better able to explain the essential features of the auditory sensations than any of its rivals. It is, of course, not improbable that this theory will need to be modified or extended in one way or another, as has been done by Wundt and by Hermann, for example, but the ground principle—the analysis of sound by resonators in the internal ear—will, it is the author's belief, endure.

SECOND SECTION

PHYSIOLOGY OF VOICE AND SPEECH

The physiology of voice and speech covers so wide a field that it will be necessary for us here to limit ourselves to the most important facts. Let it be expressly understood that what follows is to be regarded only as a brief orienting survey.

The uppermost part of the *trachea*, the *larynx*, is fashioned in a peculiar way so as to serve for the production of the voice. The most essential parts of the larynx are the *vocal cords*. These are thin, elastic bands stretched across the lumen of the larynx, and like other structures of the kind, they can be made to produce distinct tones by being set in vibration. In their case the vibration is caused by a blast of air from the lungs forced through the chink (glottis) between their free edges. The pitch and other qualities of the tones thus produced are altered by varying the tension and mode of vibration of the cords. This function it is the business of the laryngeal muscles to discharge.

§ 1. ACTION OF THE LARYNGEAL MUSCLES

The true vocal cords are attached at one end to the recurrent angle of the *thyroid cartilage* and at the other to the vocal processes of the *arytenoid cartilages*; consequently their tension and position can only be altered by changing the distance from the thyroid cartilage to the arytenoids and the distance from one arytenoid cartilage to the other.

The arytenoids are fastened to the *cricoid* cartilage, so that every movement of the latter produces a change in the position of the former; hence, the distance between the thyroid and the arytenoids can be altered by moving the cricoid.

The action of the separate muscles may be condensed somewhat as follows:

Contraction of the cricothyroid increases the tension of the vocal cords by rotating the cricoid cartilage upon the thyroid around an axis running through the articulation which the small (lower) cornua of the thyroid make with the cricoid. Thus the broad posterior plate of the cricoid to which the arytenoids are attached is moved downward and backward, and, the arytenoids being prevented by ligaments from slipping forward, as a consequence the vocal cords are put on a stretch.

The *glottis* is widened by moving the vocal processes of the arytenoid cartilages, to which the vocal cords are attached, farther asunder. This is accomplished chiefly by contractions of the *posterior crico-arytenoid* muscle springing from the cricoid cartilage and attached to the muscular processes of the arytenoid cartilages. The action of this muscle is represented schematically in Fig. 200. It contributes to the tension of the vocal cords by holding the arytenoid cartilage against the muscles which tend to draw it forward (Neuman). In this abducting action the posterior crico-arytenoid is aided to some extent by the vertically directed portion of the lateral crico-arytenoid (Rühlmann).

But for the most part the lateral crico-arytenoid is an adductor of the vocal cords (Fig. 201) and the *thyro-arytenoid* lying over this muscle has the same action.

The *vocalis* or *internal thyro-arytenoid* muscle, regarded by several authors as belonging to the thyro-arytenoid, runs from the angle of the thyroid cartilage to the arytenoid cartilage and is applied to the outer margin of the vocal cord of each side. It serves first to relax the vocal cords by approximating the points of their attachment. But a much more important function is to impart the necessary internal tension and firmness, as well as to give a favorable form and position to the whole mass of the vocal cord, for intonation (Grützner).

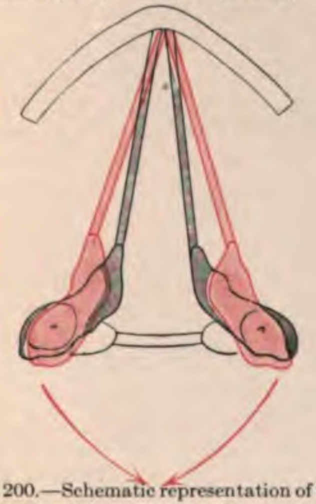

FIG. 200.—Schematic representation of the action of the posterior crico-arytenoid muscles, after Testut. The red color indicates the position of the vocal cords and of the arytenoid cartilages, when these muscles contract.

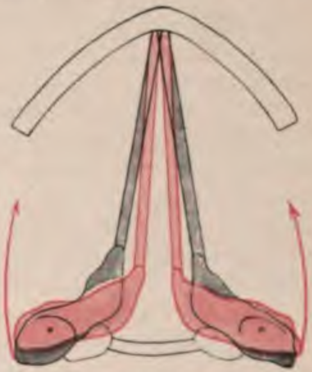

FIG. 201.—Schematic representation of the action of the lateral crico-arytenoid muscle, after Testut. The red color indicates the position of the vocal cords and of the arytenoid cartilages when these muscles contract.

With the exception of the crico-thyroid muscle which is innervated by the superior and median laryngeals, the latter arising from the pharyngeal branch of the vagus, the muscles of the larynx receive their *nerve supply* from the recurrent laryngeal.

§ 2. VOICE PRODUCTION

Production of sound in the larynx presupposes that the glottis is closed and that the vocal cords are placed in a state of tension. If then air is driven from the lungs under sufficient pressure, it forces its way through the glottis and as it does so sets the vocal cords in vibration.

Caginard-Latour and Grützner have estimated the air pressure necessary for this purpose. On patients with tracheal fistulæ they connected a manometer with the trachea by means of a tracheal cannula and demonstrated for a tone of medium height and strength a pressure of 140 to 240 mm. of water; for very loud tones, as in shouting at the top of the voice, a pressure as high as 945 mm. of water was obtained.

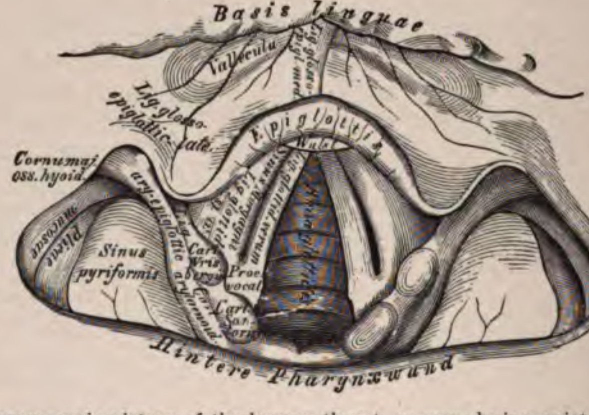

FIG. 202.—Laryngoscopic picture of the human throat, as seen during quiet inspiration. Enlarged twice (Heitzmann).

The power which produces this pressure comes from the muscles of expiration, chiefly the abdominal muscles. It is said that good singers use only the thoracic muscles of expiration.

The sound produced in the larynx is modified as to its timbre but not as to pitch, by the resonance chambers—pharynx, mouth, nasal cavities, etc.—and the task of the voice culturist, besides that of inculcating correct habits of breathing, consists merely in training the pupil to so shape these cavities as to impart the most agreeable quality.

§ 3. REGISTERS OF VOICE

Before the invention of the *laryngoscope*, our knowledge of the behavior of the vocal cords, etc., in the production of voice was based mainly on observations made with dissected preparations. But with the invention of this instrument by Garcia (1855) physiological and pathological study of the larynx entered upon an entirely new era.

The laryngoscope is a very simple instrument. A concave mirror held before the observer is provided with an aperture through which the observer looks. It receives light from some artificial source, and reflects it upon a plain mirror held at the proper angle in the pharynx. The latter mirror serves both to illuminate the interior of the larynx and to form an image of the same which can be seen by the observer.

Fig. 202 represents a laryngoscopic picture as seen in quiet breathing and Fig. 203 that seen in vocalizing.

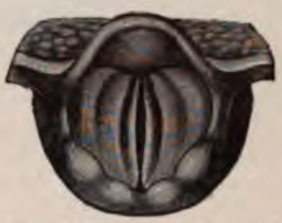
FIG. 203.—The appearance of the vocal cords while producing a chest tone, after Mandl.

Two different registers are distinguished: the chest voice and the falsetto or head voice. The former is fuller and richer—i. e., richer in lower overtones—than the falsetto. The chest tones are lower than the head tones; although within a certain compass the same person can produce identical tones with either the chest voice or the head voice.

In the production of chest tones the vocal cords vibrate throughout their entire breadth. They are also pressed inward, thus narrowing the glottis so that the air can only escape very slowly. In the production of head tones only the edges of the vocal cords vibrate and the glottis is firmly closed posteriorly, but is rather widely open anteriorly. The air escapes therefore more readily than in the case of chest tones. For this reason chest tones can be held longer than head tones.

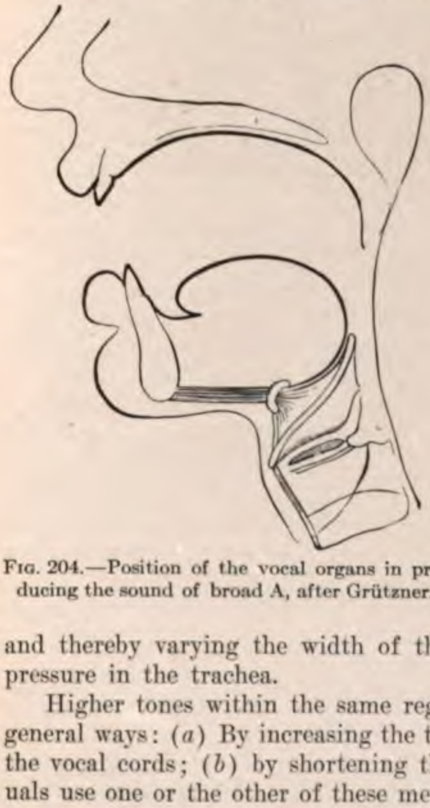
FIG. 204.—Position of the vocal organs in producing the sound of broad A, after Grützner.

We have the following means in the larynx itself of *altering the pitch* of the voice (Grützner): (1) By changing the longitudinal tension of the vocal cords; (2) by limiting the vibrating length of the vocal cords, which is done by applying the inner surfaces of the arytenoid cartilages to each other progressively more and more from posterior to anterior; (3) by changing the form of the vocalis muscle, and thereby varying the width of the vocal cords; (4) by altering the air pressure in the trachea.

Higher tones within the same register therefore may be produced in two general ways: (*a*) By increasing the tension and at the same time lengthening the vocal cords; (*b*) by shortening the vibrating portion. Different individuals use one or the other of these methods more or less exclusively.

§ 4. ELEMENTS OF SPEECH

Language is made up of words, words of syllables and syllables of elementary sounds called vowels and consonants. Vowels are produced when the voice is modified by merely changing the shape of the resonance cavities —pharynx, mouth, and nasal passages; consonants when the air or voice is more or less obstructed by the movable parts of the organs of speech— lips, teeth, tongue and palate.

In whispering the glottis is partially open and the air is allowed to pass through without setting the vocal cords in vibration. Since each of the resonance cavities has a sound of its own which it emits when the air contained in it is caused to vibrate, and since sounds may be produced by the lips, tongue, etc., alone, it is possible to speak without voice.

A. VOWELS

We cannot here discuss exhaustively the changes of the mouth cavity necessary for the production of vowels. Grützner summarized the most important of them as follows: If the voice be sounded with the tongue well down in the mouth, and the lips at first but slightly open, the sound of U (OO) is produced. Then while the voice is sounding, if the mouth be opened more and more without changing the position of the tongue the sound of OO gradually passes into that of O and finally into that of broad A, and *vice versa.* The vowels U, O, A, can be uttered therefore merely by changing the size of the mouth opening; in ordinary speech, however, the tongue and soft palate take part in the changes. If now the sound of broad A be uttered with the mouth moderately open (Fig. 204) and if without changing the size of the opening the tongue be gradually lifted more and more toward the hard palate we get successively the sounds of long A and E (Fig. 205) (German E and I). In this series the space inclosed between the larynx, posterior wall of the pharynx, soft palate and base of the tongue (laryngeal space, Purkinje) gradually becomes larger.

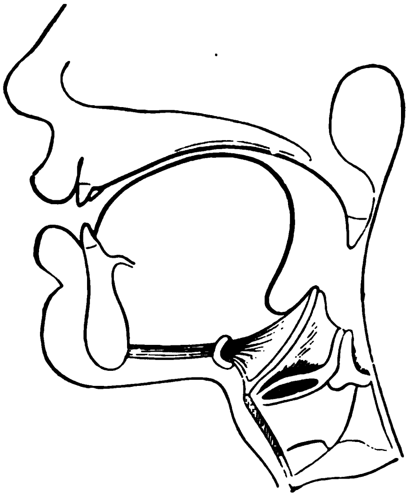

FIG. 205.—Position of the vocal organs in producing the sound of long E, after Grützner.

The other sounds of these same letters are produced by combination of the positions already mentioned for the two series. The larynx and soft palate, however, undergo changes of position also.

Donders has shown that the buccal cavity is attuned for the production of the different vowels not at the same pitch, but at different pitches. The tones which are favored by the shape of the cavity may be found by blowing into the mouth while the organs are in the proper positions; then if these tones occur as overtones in the sounds emitted by the vocal cords, they are selected by the resonance of the cavity and are intensified. According to Helmholtz (1863), each vowel has one or two such tones (the pitch of which is constant) which are characteristic of it whenever it is either sung or spoken. Those vowels which are formed when the tongue is high in the mouth, thereby dividing it into two cavities (viz., long and short A and E) have two tones, and those formed when the tongue is low (viz., OO, O and broad A) have but one.

B. CONSONANTS

The consonants are much more complicated in the mode of their production than the vowels, one important feature in their production consisting of changes in the resonance quality of the bucco-pharyngeal space. In most of the consonants the mouth and nasal cavities are separated from one another by the soft palate, but in some not. But as more or less complete obstruction of the air in some part of the passage is common to all, the distinguishing character of the sound depends on the place and manner of the obstruction. Some consonants are uttered with voice, others without.

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CHAPTER XXI

VISION

IF we wish to investigate an object by means of the tactile sense, we must be able to feel the different parts of it. In doing this different nerve fibers are stimulated; each nerve fiber produces a special sensation, which, owing to its "local sign," differs from those mediated by other nerve fibers; and the sum total of all these different sensations gives us our idea of the object.

It is the same with the eye. The retina constitutes a mosaic of nerve endings sensitive to the light; each of these nerve endings produces a sensation endowed with its own peculiar "local sign"; and just as with the skin, the total result of all these sensations constitutes our idea of the object as obtained by vision.

From this it is evident that a clear idea of an object perceptible to the eye can only be obtained, if each point of the object acts upon its own particular point of the retina.

Since light emanating from or reflected from an object radiates in all directions, becoming more and more divergent the farther it proceeds, in order to form a sharp picture of the object on the retina the light must be collected by refraction of its rays, in such a manner that they will be focused on the retina. This is the purpose of the refracting media of the eye.

The physiology of the visual organ must begin therefore with a consideration of the eye as an optical instrument. After that we shall study the visual sensations, and the movements of the eye.

FIRST SECTION

THE EYE AS AN OPTICAL INSTRUMENT

§ 1. THE OPTICAL CONSTANTS OF THE EYE

The eye contains a number of *refracting media* separated from one another by approximately spherical surfaces. These media named from anterior to posterior are: (1) The layer of tears; (2) the cornea; (3) the aqueous humor; (4) the crystalline lens composed of many layers of different refracting power; (5) the vitreous body.

In order to follow the course of light rays in the eye we must determine (1) the *refractive indices*[1] of the various media; (2) the *radii* of the refracting surfaces; (3) the *distances* of the different refracting surfaces from one another. These measurements are called the *optical constants* of the eye.

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[1] The ratio between the velocity of light in a vacuum and its velocity in a given medium, as glass, is the refractive index of that medium. Since however, the velocity in air

The following table after Helmholtz contains a summary of values found by different authors for the refractive indices of the various media in the human eye:

Cornea	1.330–1.357
Aqueous humor	1.335–1.356
Vitreous body	1.336–1.357
Crystalline lens, outer layer	1.338–1.474
" " median	1.352–1.478
" " core	1.390–1.481

The lens, as appears from the table, has a different refractive index in its different layers, the value increasing from without inward. As a consequence, the focal distances of the component lenses become smaller in the same order and the total refracting power greater than it would be, if the whole lens had the refractive index of its core (Young, Listing).

Hence it is a mistake to try to replace the crystalline lens by a homogenous lens of the same form and with an average refractive index. Such a lens must have a higher total refractive index than that of its densest part.

In calculating the course of the light rays in the eye, we shall follow Helmholtz in supposing the crystalline lens to be replaced by a homogenous lens with a refractive index of 1.4371.

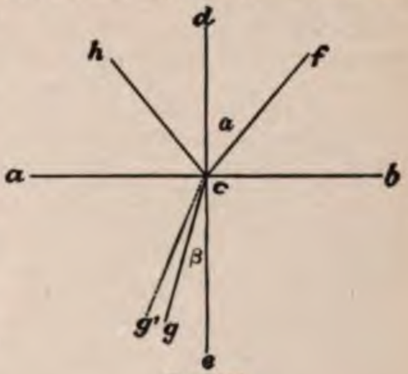

FIG. 206.

The problem to be solved is rendered much easier by this simplification and we can now treat the optical system of the eye as if it were composed of two relatively simple systems. The first consists of (1) air, (2) cornea, (3) aqueous humor; the second of (1) aqueous humor, (2) crystalline lens and (3) vitreous body.

The system of the cornea can be simplified still further for three reasons: it is very thin, its surfaces are almost concentric and its refractive index is only a little greater than that of the aqueous humor. Since the refractive index of the layer of tears on the outside differs but slightly from that of the aqueous humor inside, we may think of the cornea as a watch-glass-shaped

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is but slightly less than in a vacuum, the refractive index of a medium is ordinarily given as the retardation which the light suffers in passing from air into that medium. The refractive index may be found by measuring the angle of incidence and the angle of refraction—e. g., the angles α and β formed by the light ray $f\ g$ in Fig. 206. The refractive index of the medium below the line $a\ b$, supposing the medium above that line to be air, is given by the formula $n = \frac{\text{sine } \alpha}{\text{sine } \beta}$.

lens immersed in aqueous humor. Such a lens does not change the course of the light rays to any appreciable extent. According to an estimate of Helmholtz the focal distance of the cornea embedded in the aqueous humor would be 8.7 m., a distance which, in comparison with the dimensions of the eye, can be regarded as practically infinite.

The first refracting system is reduced therefore to a simple optical system composed of two media, the air and the aqueous humor, separated by a surface with the curvature of the cornea.

To be able to follow the course of the light rays in the eye we need therefore, in addition to the refractive indices already mentioned, only the following data: (1) The radius of curvature of the cornea; (2) the distance of the anterior surface of the lens from the vertex of the cornea; (3) the radius of curvature of the anterior surface of the lens; (4) the thickness of the lens and (5) the radius of curvature of the posterior surface of the lens.

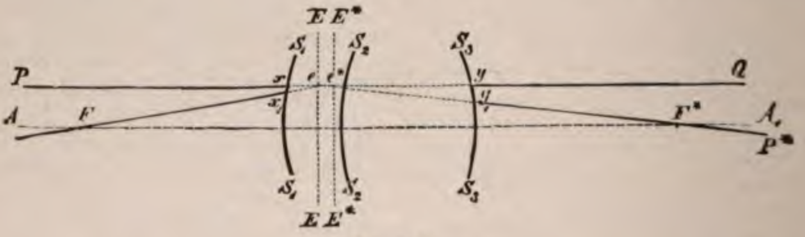

Fig. 207.

Some of the values found by different authors for these dimensions are given in the following table:

(1) Radius of curvature of the anterior surface of cornea	6.852–8.154	mm.
(2) Distance from vertex of cornea to anterior surface of the lens	2.900–4.09	"
(3) Distance from vertex of cornea to posterior surface of lens	6.844–7.69	"
(4) Radius of curvature of anterior surface of lens	7.860–12.58	"
(5) Radius of curvature of posterior surface of lens	5.13 –8.49	"

To enable us the better to follow light rays through an optical system like that represented by the human eye, let us suppose the refracting surfaces S_1, S_2 and S_3 in Fig. 207 to be related to each other as are the refracting surfaces of the cornea and lens. The points F and F^* will be the anterior and posterior focal points of the entire system, the line AA_1 its axis. Imagine any incident ray parallel to the axis to be represented by Px. Since all rays parallel to the axis pass through the focal point, whatever course this ray may take through the system, we know that after it is refracted it will pass through the focal point F^*. But the incident and refracted rays must meet somewhere if prolonged. Let this point of meeting be e^*. Imagine the incident ray Px projected toward Q and call the portion e^*Q the incident ray. Since this is everywhere parallel to the axis it must have a corresponding ray which will pass through the anterior focus F. Prolonging the incident ray until it meets the refracted ray again, we get the point e.

The rays Px and Fx_1, therefore, converge toward the point e, the rays Qy and F^*y_1, toward e^*—i. e., if we regard e as a luminous point e^* will be its image.

If through these points two planes be drawn perpendicular to the axis of the system, then every point in the plane e will have its image in the plane e^*, and the image will be on the same side of the axis and at the same distance from it. In short an object in the plane e has an erect image of the same size in the plane e^*.

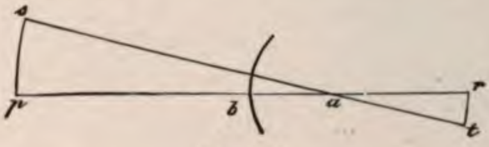

Fig. 208.

These two planes are called the principal planes of the system and the points at which they cut the optical axis are called the *principal points.*

All distances in general are calculated from the principal points, those which concern the incident ray from the first, those which concern the refracted ray from the second.

Now what will be the relation between an object, whose rays are transmitted by a system of this kind, and its image? The answer is, just the same relation as between the object and image of a simple system.

If—e. g., in Fig. 208, which represents a simple optical system—an object, *sp*, be transmitted by a simple refracting surface, the size of the image, *tr*, will be to the size of the object as *ar* is to *pa* (from the similar geometrical figures *asp* and *art*). The point *a* of such a system is called the nodal point.

So also in Fig. 209 where EE^* are the principal points and F and F^* the focal points, there will be two points K and K^* so situated (at equal distances from E and E^*) that the size of the object PA will be to the size of its image P^*A_1 as the distance AK is to the distance A_1K^*. These two points are called the *nodal points* of the system. They may be defined as the two points so situated that a ray directed toward the first will be directed toward the second after refraction, the rays before and after refraction being parallel.

It is evident that if we can locate accurately the *nodal points* of the eye and know the size and distance of any object, we can estimate the size of its image in the eye. Moser was the first (1844) to make use of theoretical results obtained by Gause and Bessel and on the basis of these to calculate the position of the two nodal points. Somewhat later Listing gave an estimate of the numerical values according to the best measurements completed at that time. Since his time the designation of *schematic eye* has been applied to an eye whose optical constants correspond approximately to the mean value

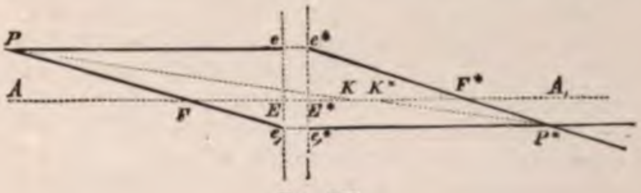

Fig. 209.

of the prevailing measurements. It must be observed, however, that, as will appear from the table on page 510, the individual variations are considerable.

In the following table are contained the *optical constants* from two schematic eyes, which have been calculated by Helmholtz on the basis of newer measurements.

The location is in all cases given as the distance in millimeters from the vertex of the cornea, and is reckoned as positive when it is posterior and negative when anterior.

Directly Determined

	I.	II.
Refractive index of the aqueous humor and vitreous body.	1.3376	1.3365
Total refractive index of crystalline lens	1.4545	1.4371
Radius of curvature of the cornea......................	8.0	7.829
Radius of curvature of the anterior surface of the lens....	10.0	10.0
Radius of curvature of the posterior surface of the lens ...	6.0	6.0
Location of the anterior surface of the lens	3.6	3.6
Location of the posterior surface of the lens.............	7.2	7.2

Calculated

	I.	II.
Cornea: anterior focal distance	23.692	23.266
Cornea: posterior “ “	31.692	31.095
Lens: focal length	43.707	50.617
Posterior focal distance of the eye	19.875	20.713
Anterior “ “ “ “ “	14.858	15.498
Location of the I principal point	1.9403	1.753
“ “ “ II “ “	2.3563	2.106
“ “ “ I nodal point.........................	6.957	6.968
“ “ “ II “ “	7.373	7.321
“ “ “ anterior focal point	−12.918	−13.745
“ “ “ posterior focal point....................	22.231	22.819

In Fig. 210 these values are brought together in a diagram of the human eye enlarged about three times. We see that the principal points ($h_{,}$ $h_{,,}$) lie in the middle of the aqueous chamber and the nodal points ($k_{,}$ $k_{,,}$) in the posterior part of the crystalline lens. The posterior focal point $F_{,,}$ falls upon the retina.

By means of these so-called *cardinal points,* the path of any given incident ray can be determined, as has been seen on page 511, beyond its last refraction; likewise, the location of any point occurring in the neighborhood of the axis. Since, moreover, the two principal points and the two nodal points lie very close together (by the above table, 0.416 mm. and 0.353 mm. apart respectively), for many purposes the two can be regarded as one point and the eye reduced to a single optical system. In this *reduced eye* the principal point lies (according to Listing's scheme) 2.345 mm. posterior to the anterior surface of the cornea and the single nodal point 0.476 mm. anterior to the posterior surface of the lens. If from this point a curve be drawn through the reduced principal point (radius of 5.125 mm.) it will represent the anterior limiting surface of the reduced eye; in front of it is air, back of it aqueous humor or the vitreous body.

As appears also from the above table, the *anterior focal distance* of the cornea (II eye) is 23.3 mm., that of the entire eye 15.5 and the focal length of the lens 50.6 mm. The refracting power of the cornea is therefore 43.2 diopters[1] (1,000 ÷ 23.3), that of the entire eye 64.5 diopters.

It follows that the strongest refraction of light takes place in the cornea.

Occasionally among old people the lens becomes turbid and opaque. In order to restore the sight in such cases the lens is removed. After the operation the refracting power of the eye, which can no longer be accommodated, is about 10 D. less than before—i. e., in the normal eye of old persons the lens raises the refracting power of the eye by about this amount.

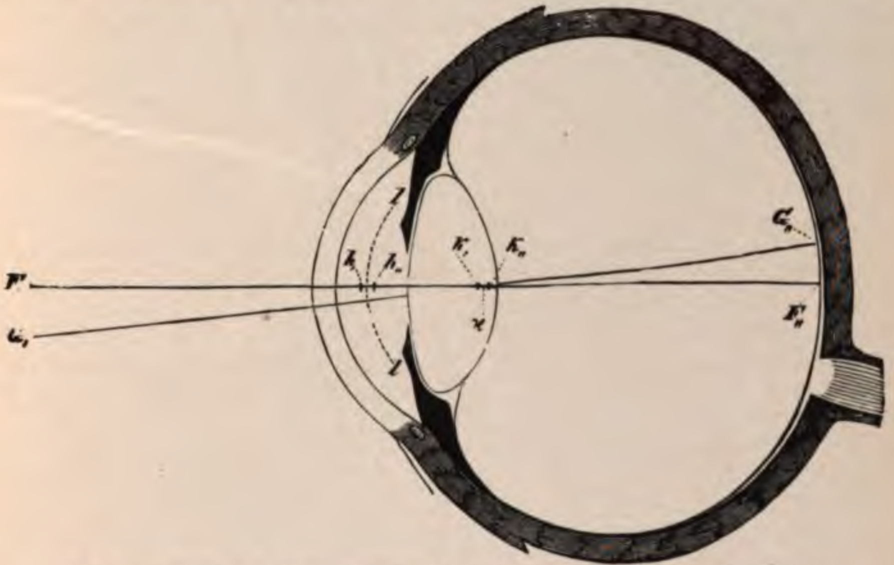

Fig. 210.—Position of the cardinal points in the schematic eye, after Helmholtz.

§ 2. IMAGES UPON THE RETINA

The size and position of an image formed by a centered optical system depends not only upon the size and position of the object, but also upon the position of the cardinal points of the system. From Fig. 209 it is evident that so long as the distance $e\ P > F\ E$ the image will be *inverted*—i. e., so long as an object is beyond the outer or anterior focal point of the eye the image on the retina will be inverted. Again, so long as $e\ P > 2\ F\ E$ the image will be smaller than its object or, applied to the eye, so long as the object is more than twice the distance of the outer focal point from the eye, the image on the retina is *smaller* than the object. This tallies with our experience that we cannot focus sharply on the retina rays from objects lying nearer the eye than twice its focal distance.

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[1] One diopter (D) is the refracting power of a lens with a focal distance of 1 meter: the refracting power is the reciprocal of the focal distance.

A. DIRECT AND INDIRECT VISION

When we wish to scrutinize an object very closely, we so direct the eye that the middle point of the object is pictured on the *fovea centralis* of the yellow spot in the retina. This point is therefore designated as the *center of exact vision.* The diameter of the fovea according to Fritsch is 1–1.5 mm., so that it corresponds to a visual angle (see page 517) of 4°–6°.

The nervous elements of the retina, however, reach all the way to the *ora serrata,* and, being also sensitive to light, can produce conscious sensations from all parts. But these sensations, as compared with those aroused from the fovea, are more and more indistinct the farther the retinal cells affected lie from the fovea.

The reader can convince himself of this by a very simple experiment. If one eye be closed and the other be directed intently at some object, he will find that of all the objects in the room only that one directly regarded and those lying nearest it are seen distinctly, others appear less and less distinct the farther they are situated from the line of vision. Vision with those parts of the retina lying outside the fovea centralis is called indirect vision.

Indirect vision is of very great service, for by it we obtain some idea of the space in which the object directly regarded is situated. Especially is it of service in walking, as anyone can prove to himself by trying to walk over an unfamiliar path with one eye closed and with indirect vision of the other excluded by looking through a tube or through the half-closed hand. He finds it difficult either to perceive or to avoid obstacles. In fact even close work, such as reading a printed page, is much more difficult under such circumstances, because only a small part of the print can be seen at one time.

B. THE LIGHT-PERCEIVING LAYER OF THE RETINA

The retina consists of several different elements, part of which are nervous in nature and part serve as a supporting substance for the nervous structures. Ramon y Cajal has published not long since a detailed investigation of the structure of the retina. His chief results so far as the nervous elements are concerned, may be summarized briefly as follows (cf. Fig. 211):

> The *rod fibers* (*b b*) whose bodies together with those of the cones, constitute the outer granular layer (*B*) end inwardly in little knots embraced by the terminal fibers of the outer processes of the definitive bipolar cells (*c*). These cells together with those belonging to the cones constitute the inner granular layer (*E*); their outer tuft of dendrites is directed vertically. Below the bipolar cell rests upon a ganglion cell (*n*) and clasps it with fingerlike branches. These ganglion cells form the so-called ganglion-cell layer (*G*).
>
> The *cone fiber* (*a*) ends in a broad base, from which short basilar dendrites are given off. With these the dendrites of the spinal bipolar cells (*e*) belonging to the cones come into contact. The outer tuft of dendrites of these bipolar cells, in contrast with that of the bipolar cells belonging to the rods, is quite flat, and widely spread out. The inner process ends at various levels of the inner plexiform layer (*F*) in a terminal arborization which comes into relation with the outwardly directed branchlets of definite ganglion cells.

From the cells of the ganglion layer optic fibers are given off, forming the innermost layer of the retina, the nerve-fiber layer (*H*).

The lateral extent of the outer tuft of dendrites of the bipolar cells (*E*), both of those which correspond to the rods and those which correspond to the cones, varies greatly. In general several rods or cones are connected with each of the bipolar cells. But each cone of the fovea centralis is in contact with the dendrites of but one bipolar cell.

Compared with the end arborizations of the ganglion cells those of the bipolar cells are very small; consequently the smallest ganglion cells must be in touch with a relatively large number of bipolar cells.

In addition to these elements the retina contains still other cells of a nervous nature, lying either in the inner granular layer (outer and inner horizontal cells) or in the inner plexiform layer (amacrine cells, *h*). The former, according to Cajal, are for the purpose of bringing definite groups of rods into relation with other definite groups more or less remote from them. Nothing positive can be said as to the significance of the amacrine cells.

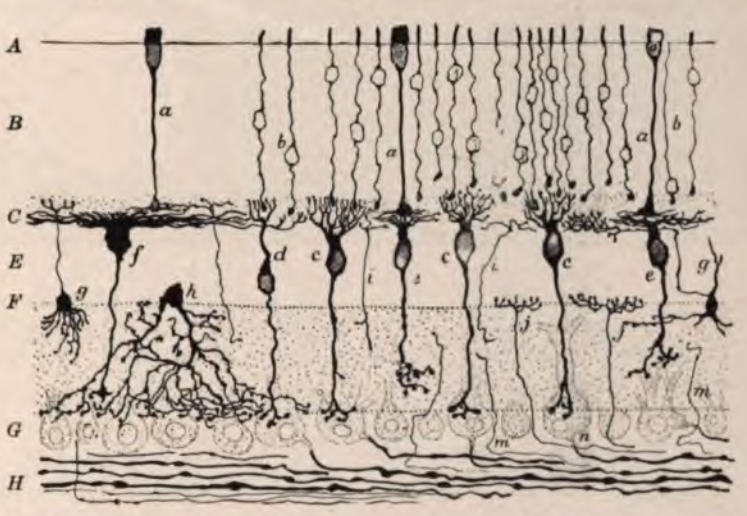

FIG. 211.—A section through the retina of a full-grown dog, after Cajal. *A*, layer of rods and cones; *B*, outer granular layer, containing the bodies of the visual cells; *C*, outer plexiform layer; *E*, inner granular layer, containing the bipolar cells; *F*, inner plexiform layer; *G*, ganglion cell layer; *H*, layer of the optic fibers. *a*, cone fiber; *b*, body and fiber of a rod cell; *c*, bipolar cell with "brush" of fibrils belonging to the cones; *f*, giant bipolar cell with wide spreading brush of fibrils; *h*, diffuse amacrine cell, the varicose processes of which lie for the most part directly on the ganglion cells; *i*, ascending nerve fibers; *j*, centrifugal fibers; *g* and *g′*, specialized cells which are seldom impregnated; *n*, ganglion cell receiving within it the terminal brush of a bipolar cell from the rods; *m*, nerve fiber which is lost in the inner plexiform layer.

Finally, the retina contains also centrifugal nerve fibers (*j*).

Which of these layers of the retina is the one primarily acted upon by the light?

Certainly not the nerve-fiber layer, for the optic nerve is just as insensitive to light as other nerve trunks. This is shown especially by the following experiment first performed by Mariotte (about 1665).

If the left eye be closed and the right be fixed steadily on the white cross in Fig. 212 and the book be held at a distance of about 25 cm. from the eye, the white circle will disappear entirely from view, so that the black field appears uniform. There is, therefore, in the eye a spot which is not sensitive to light, and which is called for this reason the blind spot.

By measuring the apparent size of the *blind spot*, and its apparent distance from the fixation point of the eye, it can be shown to correspond exactly with the point of entrance of the optic nerve, where the mass of optic fibers, not covered by the black pigment, spreads outward toward the transparent media of the eye. The insensibility of the optic nerve fibers appears still more directly, if by means of a small mirror the light of a small flame be thrown into the eye so that it falls upon the point of entrance of the optic nerve. The subject experiences no sensation of light (Danders).

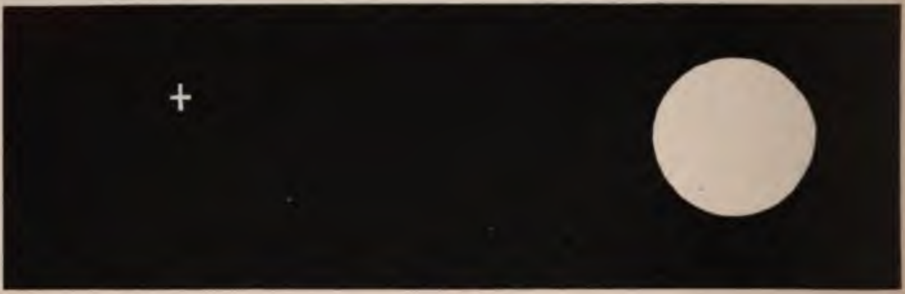

FIG. 212.

The blind spot is so large that at a distance of 1.7–2 m. it can contain the image of a man's head. The reason why we do not ordinarily miss the object in our field of vision which falls upon the blind spot is, that we unconsciously fill the gap with something conformable to the rest of the field. Moreover the distance of the blind spot from the center of exact vision is such that objects in that quarter would be pretty indistinct if the spot were not blind.

The light-perceiving layer of the retina, therefore, must lie behind the nerve-fiber layer, or still more accurately behind the blood vessels of the retina, as was first shown by the famous experiment of Purkinje.

If a beam of light from a short-focus lens be concentrated on the conjunctiva of one eye as far as possible from the cornea, and at the same time the gaze of this eye be directed toward a uniformly colored dark background, there appears at once in the field of vision a network of dark, branching vessels. This network is nothing else than the shadow of the vessels of the retina.

Purkinje's figure, as this vascular tree is called, is rendered still more plainly visible if the illuminating lens be moved to and fro; it can also be perceived, if while the gaze is directed to a dark background a burning candle be moved to and fro at one side and a little below the eye.

From the fact that we can perceive the shadow of the retinal vessels in our own eyes, it follows that the vessels themselves are in front of the light-perceiving layer of the retina. Finally, by exact physiological measurements, H. Müller has shown that the distance between the vessels and the light-perceiving layer must be from 0.17–0.33 mm., and microscopical measurements in turn have shown that the distance (0.2–0.3 mm.) takes us to the layer of rods and cones. Hence it follows with great probability that the latter structures, the *rods and cones, are the light-perceiving parts* of the retina.

Why do we not ordinarily see the Purkinje figures? Since the field of vision is always filled by objects which give more or less light to the eye, the pupil may be looked upon as a luminous disk throwing light upon the retina. Now the branches of the central vein of the retina are only about 0.038 mm. in thickness; and with a pupillary diameter of 4 mm., the umbra of these branches would be only 0.17 mm. long and so would not quite reach the sensitive layer of the retina. The penumbra which does reach the rods and cones remains always in the same place and we have become so accustomed to its presence that we do not perceive it. In Purkinje's experiment, on the other hand, the shadow falls on an unusual place and the illuminated point has a smaller diameter than the pupil, both of which circumstances tend to favor its perception in consciousness. If the source of light be not moved the figure disappears shortly, only to reappear when the source of light is again moved, just as other objects are more readily perceived when moving than when at rest.

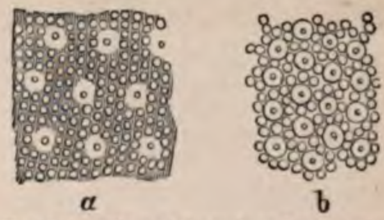

FIG. 213.—View of the rods and cones seen from the outer surface of the retina, after Max Schultze. *a*, arrangement of rods (small circles) and of cones (double circles) in most parts of the retina; *b*, arrangement in the region of the macula lutea.

Another circumstance which strongly favors the light-perceiving function of the rods and cones is the fact that the other retinal layers gradually thin out toward the yellow spot, so that in the very center of the fovea itself only cone cells are left. These are connected with the other layers of the retina by oblique, lateral branches (cf. Fig. 211).

Seen from the outside the layer of rods and cones forms a mosaiclike surface (Fig. 213), an arrangement well adapted to a light-perceiving function; for every object perceptible to the eye is transformed by refraction into a mosaic picture of itself.

C. VISUAL ANGLE AND THE LIMITS OF VISION

When the eye receives light from a luminous point, for whose distance it is not exactly accommodated, the light proceeding from the point is brought to a focus in front of or back of the retina, and an illuminated circular field (dispersion circle) is formed on the retina, the size of which depends upon the location of the focus. If the focus of the beam is close to the retina, either in front or behind it, the dispersion circle will be small; if farther from the retina, the circle will be larger.

All rays which pass through the pupil take a course in the *vitreous body* as if they proceeded from the picture of the pupil which the lens throws back into the vitreous body. The actual size of the pupil therefore is, other things being equal, the factor determining the size of the dispersion circle.

We have already seen (page 511) that the position of the retinal picture of a luminous point can be determined in the schematic eye by drawing a straight line from the objective point to the first nodal point and another parallel to this from the second nodal point to the retina. In the reduced eye the two nodal points coincide and the retinal image falls where a line from the object through the nodal point meets the retina. Lines of this kind by which the location of the image on the retina can be determined are called *lines of direction.*

That particular line of direction which connects the middle point of an outer object with the center of the fovea in the retina is called the *line of vision.*

The lines of direction enable us to determine the size of the image of an object formed on the retina. We have only to draw lines of direction from the extreme ends of the object and solve the similar triangles thus formed (see page 511). By such a construction also we can calculate approximately the distance from each other of the images of two luminous points which are just distinguishable, and can thus obtain a measure of the acuteness of vision. For several reasons, however, this linear measure is not used, but instead the angle which the two lines of direction subtend (Fig. 214) at the first or second nodal point. This angle is called the *visual angle.*

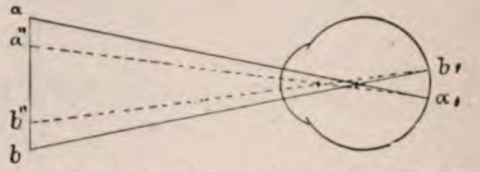

FIG. 214.—Diagram showing the visual angle, i. e., the angle subtended by two lines of direction a'' a' and b'' b' through the first nodal point.

According to an old statement by Hooke, two stars whose apparent distance from one another is less than thirty celestial seconds always appear as one star, and scarcely one person out of a hundred can distinguish the two if their apparent distance is less than sixty seconds. Later observers have obtained values varying all the way from fifty to ninety seconds.

In Listing's schematic eye a visual angle of sixty seconds corresponds to a distance on the retina of 0.00438 mm. Microscopical measurements find the thickness of the cones in the yellow spot to be from 0.0054–0.0045 mm. (Kölliker) to 0.0036–0.002–0.0015 mm. Counts of the number of cones in the fovea made by Salzer gave for the eyes of stillborn children 13,200–13,800 per square millimeter.

The *limits of vision*—i. e., the ability to distinguish two points—therefore depend upon the diameter of the cones in the center of exact vision. To be able to perceive points as distinct and separate, they must fall upon cones which are separated by at least one resting cone.

§ 3. STATIC REFRACTION IN THE EYE

The laws of refraction in an optical system teach us that for every different position of the object the position of the image changes. For this reason in order to take a picture on a sensitive plate by means of a camera, the position of the plate must be adapted to the distance of the object.

But if the plate is immovable, as is true of the retina, a nearer object can be focused by using a stronger lens—i. e., by increasing the refracting power of its system. This is what happens in the eye. By *accommodation* (see § 6), the refractive power of the crystalline lens can be increased to different degrees, so that objects at widely different distances can be focused sharply on the retina.

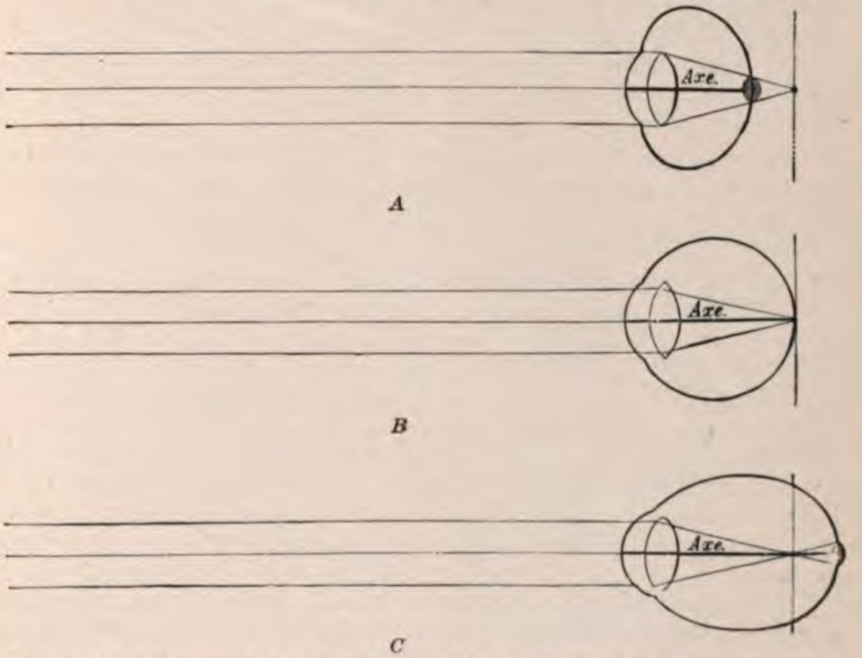

FIG. 215.—The static refraction of : *A*, a hypermetropic eye; *B*, an emmetropic eye; and *C*, a myopic eye.

An optical system is characterized by the distance of its *posterior focal point*; and we can distinguish three kinds of eyes according as the posterior focal point is *on* the retina, *in front* of or *behind* the retina (Donders). Unaccommodated eyes with the posterior focal point on the retina are to be regarded as normal and are called *emmetropic* (Fig. 215, *B*).

Eyes of the second kind where the focal point of parallel rays falls in front of the retina are called *myopic* or nearsighted, because they are only able to focus on the retina such light rays as come from objects at a finite distance (Fig. 215, *C*).

Eyes of the third kind, where the focal point falls behind the retina are called *hypermetropic*, or long-sighted (Fig. 215, *A*). In order that incident rays may be brought to a focus on the retina of such an eye, they must already be convergent as they enter the eye. Since, however, converging rays never occur in nature, it is evident that a hypermetropic eye, not provided with artificial lenses, can focus parallel or divergent rays accurately only by accommodation; in short, the hypermetropic eye, if it is to see without glasses must always be accommodated.

Of the three kinds of eyes the emmetropic is without doubt the best adapted to its purpose; for, as we have seen, rays from objects more than 5 m. distant may be regarded as practically parallel for the eye so that the unaccommodated emmetropic eye can form a distinct picture of all such objects. The hypermetropic eye can adjust itself for far distant and near objects by accommodation. But the myopic has no means at all of adjusting itself for distant objects and from this point of view at least must be regarded as the least serviceable of the three.

The *far point* of the eye is that point from which proceed light rays with the least divergence that can be focused by the eye. In the emmetropic eye the far point lies of course at an infinite distance. The far point of the myopic eye lies at a finite distance in front of the eye. The far point of the hypermetropic eye lies behind the eye. It represents the point of convergence of those rays which, after refraction in the unaccommodated eye, are brought to a focus on the retina.

We say therefore with reference to its structure that the refracting power of the myopic eye is too strong, that of the hypermetropic eye too weak.

By suitably chosen lenses both the myopic and the hypermetropic eye can be made to focus parallel rays on the retina. If we place before a myopic eye a double concave lens of such a strength as to give the parallel rays the direction they would have if they came from the far point of the eye, it is evident that now the combination, lens + the eye, affects parallel rays, just the same as does an emmetropic eye.

If we place before a hypermetropic eye a double convex lens which converges parallel rays to its far point, then the combination, lens + the eye, must again be equal to the emmetropic eye.

The *degree* of myopia or hypermetropia is measured by the refracting power of the lens necessary to make the eye emmetropic. It is evident at once that the focal point of this lens coincides with the far point of the eye and the degree of myopia or hypermetropia is therefore expressed by the reciprocal value of the distance of the far point from the eye. This correction lens determines also the *static refraction* of the eye—i. e., the amount of refraction taking place without accommodation.

§ 4. OPTICAL DEFECTS OF THE EYE

In our discussion thus far we have silently assumed that the eye is a perfectly constructed optical instrument—that its refracting media are perfectly transparent, their surfaces exactly spherical and the centers of curvature of the various media all in the same straight line. Strictly speaking, however, this is not the case, for the eye presents a number of optical defects, some of which in the majority of cases are quite negligible, while others occasionally affect its functional power to a very great extent. We shall have space here to discuss only the most important of these defects.

A. TRANSPARENCY OF THE MEDIA OF THE EYE

When we remember how complicated is the structure of the cornea and of the lens, it will not appear strange that these media are found not to be perfectly transparent. If a strong beam of light be thrown into the eye by means of a convex lens, the illuminated part of the cornea and of the lens immediately becomes visible—i. e., these structures send out from all points an irregularly diffuse light. This diffuse light likewise passes to the retina, excites it and produces a mist of light within which the images regularly formed on the retina appear enshrouded. With ordinary illumination we do not perceive this mist and it does not interfere with vision, but one may be made aware of its existence in the following manner: If in the evening a person direct his gaze away from the artificial light and toward a dark corner, the differences of light and shadow from this quarter are much more readily perceptible than equal differences coming into the eye from the direction of the source of light. The reason is that the mist of light thrown into the eye in the latter case by the highly illuminated pupil interferes with the contrast effects necessary to perception of such differences. Accordingly, when one wishes to distinguish slight differences of light and shade, he instinctively turns his back to the source of light.

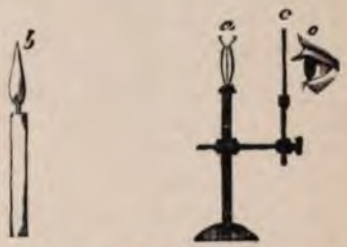

Fig. 216.—Method of demonstrating entoptic phenomena in one's own eye, after Helmholtz.

There also exist in the eye certain *flecks* which under certain circumstances may interfere considerably with perfect vision, especially if they lie in the posterior part of the vitreous body. The perception of these flecks in the transmitting media is described as *"entoptic" phenomena.* We have already had an example of such phenomena in Purkinje's figure (page 516).

Under ordinary circumstances these small dark flecks are not noticed; the reason is that an almost uniform amount of light enters the eye through every portion of the pupil, and thus the entire pupil constitutes the illuminating surface alike for all parts of the posterior portion of the eye. The flecks being smaller than the pupil, the shadows cast by them are naturally very short and do not ordinarily reach the retina.

The following method (Helmholtz) may be used for demonstrating these entopic phenomena. A convex lens of large aperture and short focal distance (*a*, Fig. 216) is placed before the eye; at some distance in front of the lens is placed a candle, *b*, a small image of which is formed by the lens at its focal point. Then a small screen, *c*, with a minute opening, is so placed that the reduced image of the flame falls in the opening. If the image lies in the anterior focal point of the eye, the rays from it which enter the eye will be parallel after refraction and a shadow of any object (b, in Fig. 217) in the vitreous body which is formed on the retina (β) will be of the same size as the object itself.

B. FORM OF THE REFRACTING SURFACES

To be able to judge the eye as an optical instrument we must have more detailed information of the actual form of the refracting surfaces. Our knowledge along this line is limited for the most part to the cornea, which, however, as we have already seen, is the most important of the refracting media (cf. page 513).

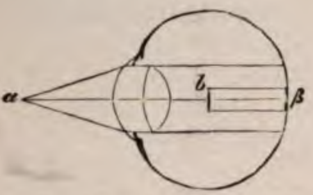

Fig. 217.—After Helmholtz.

The most exact study of this subject we owe to Gullstrand who used the following method. A disk with concentric circles (Placido's keratoscope) is so placed as to be reflected by the cornea; the reflected image is photographed by the instantaneous method; and the distances of the circles from one another are measured on the photograph. Knowing the corresponding differences on the object and the distance of the latter from the cornea, the radius of curvature of the different sectors of the cornea can be calculated.

We find as a result of this method that the optical zone of the cornea—i. e., that part immediately in front of the pupil—always approaches the spherical in form, but that it is often less sharply curved in one meridian than another. Instead of being the segment of a sphere with a circular cross section, it is then a dome with an oval cross section.

If the surface of the cornea were always perfectly spherical, it would share with all such surfaces the defect of *spherical aberration* (Fig. 218). It will be evident from the figure that spherical aberration can be corrected by flattening the refracting surface at the periphery enough to bring the several foci together. Gullstrand has found from his detailed study of the curvature of the cornea, that, as a matter of fact, the spherical aberration in the vertical plane is slightly offset by a flattening directly above the line of vision, which is probably due to the pressure of the upper eyelid. Elsewhere the flattening is not sufficient to affect the aberration. Hence we may say that that part of the cornea which is used for direct vision exhibits this defect.

C. ASTIGMATISM

When the optical zone of the cornea is not perfectly spherical but is curved more sharply in one meridian than another, the refraction of light will not be equal in the two meridians. If this difference is slight there will be no disturbance to vision; but it not infrequently happens that the asymmetry of structure is great enough to interfere with the ability to focus correctly.

A beam of light which is not brought to a single point after refraction, but has different focal distances for different meridians, is described as *astigmatic*. If the two meridians in which the focal distance is greatest and least are perpendicular to each other, the astigmatism is described as regular. We shall discuss only this kind of astigmatism here.

An astigmatic beam may be formed in two ways: (1) When the optical system is asymmetrical and the incident rays vertical; and (2) when the optical system is symmetrical and the incident rays oblique.

The first case is the simplest (for the second see page 525). Suppose we have a lens, which in the horizontal meridian has a refractive power of 10 diopters; in the vertical meridian a refractive power of 12 diopters. It is evident that the beam after refraction will no longer have a common focus, for the incident rays in the horizontal meridian are brought to a focus $\frac{1}{10}$ m. behind the lens and those falling in a vertical meridian $\frac{1}{12}$ m. behind the lens.

Further study of the problem has shown that if no account be taken of the spherical aberration, the light rays instead of being converged to foci at the focal points of the two meridians are converged into a focal line perpendicular to the principal ray at each of those points. The first focal line corresponds to the focal point of the meridian with the strongest refractive power and is perpendicular to that meridian—i. e., in the plane of the weakest meridian. The second focal line corresponds to the focal point of the weakest meridian and is perpendicular to that meridian—i. e., in the same plane as the strongest meridian.

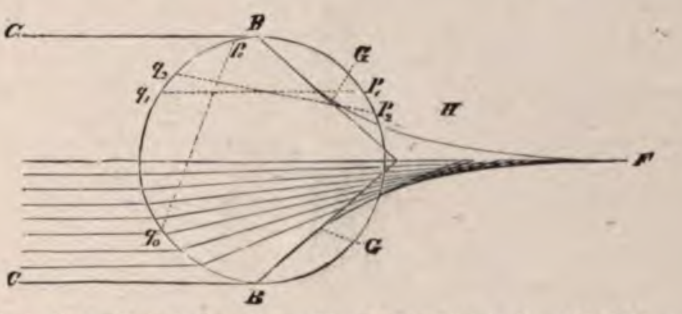

FIG. 218.—Illustrating spherical aberration. The rays parallel to the axis of the system are converged to foci nearer and nearer the convex surface the farther they are removed from the axis.

In front of the first focal line the beam of rays forms in a cross section an ellipse with the longer axis in the direction of the first focal line, beyond the second focal line the beam forms an ellipse with the longer axis in the direction of the second focal line. A transition from the one elongation to the other takes place between the two focal lines, the upright ellipse becoming first a circle and then a procumbent ellipse (Fig. 219).

In an astigmatic eye, therefore, a homocentric[1] bundle of rays cannot be brought to a single focus. When the eye is adjusted for the most refractive meridian, the images on the retina are all drawn out in the direction of the first focal line; when it is adjusted for the least refractive meridian the retinal images are drawn out in the direction of the second focal line—in both cases, therefore, distorted. To prevent this the eye is adjusted so that some point between the two focal lines falls on the retina. The distortion of objects is thereby rendered less, but the distinctness of the image is more or less reduced.

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[1] That is, rays proceeding from a common point or rays which pass through a common point when prolonged.

Astigmatism may be demonstrated subjectively by the use of a chart (like that in Fig. 220) composed of several radii, all of the same width and depth of color. If this chart be held before the eye at such a distance that only one meridian can be seen distinctly, this meridian corresponds in direction to the most refractive meridian of the eye, and its image on the retina to the second focal line. If now the chart be brought as close to the eye as possible, again only one meridian is distinct. In regular astigmatism this meridian is at right angles to the first: it gives the direction of the least refractive meridian of the eye and its image corresponds to the first focal line.

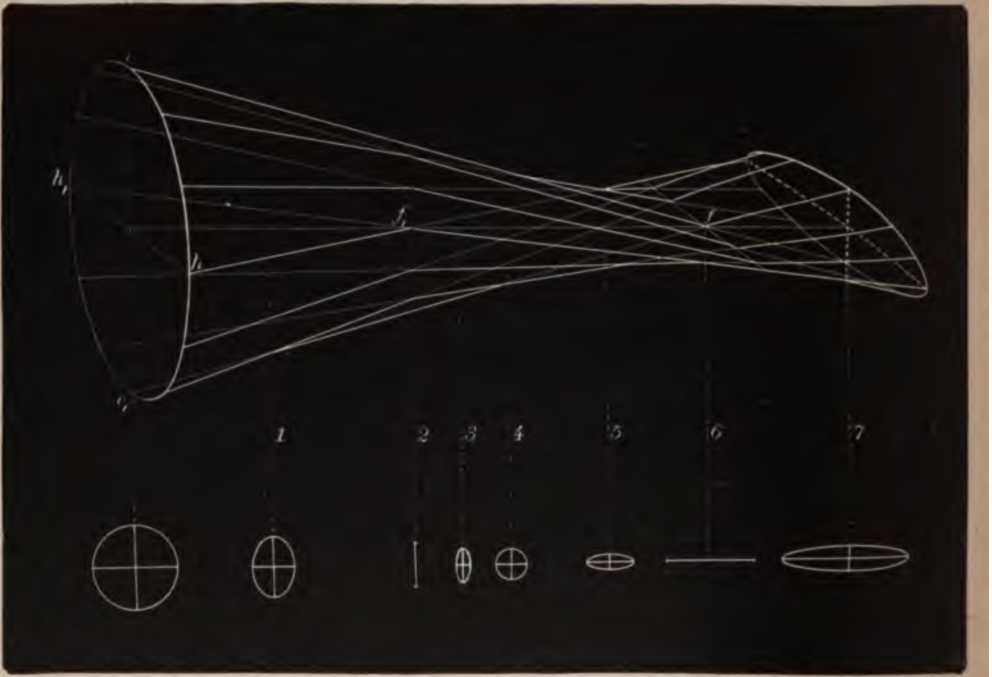

FIG. 219.—Refraction of the light rays in regular astigmatism, showing the form of a beam at different cross sections, after Fuchs, $v\,v_{,}$, vertical meridian of the cornea; $h_{,}\,h$ the horizontal meridian. The focus for the horizontal meridian is at $f_{,}$; that for the vertical meridian at f; the image of a point is, therefore, not a point but a dispersion circle. The shape of the circle, however, is determined by the spot at which the retina is situated. At the position 2, the image of a point would be a vertical line, at 4 a circle, at 6 a horizontal line, etc.

A certain degree of astigmatism occurs in all eyes, although, as a rule, it is so slight as to have no practical importance. The astigmatism which causes a noticeable distortion of images is caused mainly by the asymmetrical structure of the cornea.

As a rule, however, the actual astigmatism of the cornea is greater than the total astigmatism as determined by the subjective method. This means that it is compensated to some extent by some structures in the eye itself—as, e. g., the lens.

According to measurements made by Nordenson on pupils between the ages of seven and twenty, out of 452 eyes examined only 42 (nine per cent) had no astigmatism of the cornea which could be detected. Sixty-nine pupils had an astigmatism of more than 1 diopter, and four an astigmatism of more than 1.5 D. However, a normal acuteness of vision is perfectly possible with an astigmatism of 1.5 diopters. In 85.1 per cent of the astigmatic eyes examined the vertical meridian was the most refractive; in 1.5 per cent the horizontal, and in 13.4 per cent an oblique meridian. In the majority of cases therefore the vertical meridian is the most sharply curved.

The difference in static refraction between the most refractive and the least refractive meridian of the eye, expressed in diopters, is known as the *degree of astigmatism*. After this has been determined (by methods which we cannot discuss here) it can be corrected by means of cylindrical lenses—i. e., glasses which represent segments of the curved surface of a cylinder.

In using such glasses for the correction of astigmatism the glass is so placed that its own asymmetry is the reverse of that of the eye. Suppose an eye were myopic in the vertical meridian and emmetropic in the horizontal. Then the eye could be made emmetropic by placing before it a suitable concave-cylindrical glass with a curvature in the vertical meridian. The myopia in this meridian would be corrected by the curvature. Rays falling in the horizontal meridian would not be refracted at all, and would not need to be, for the eye we suppose is already emmetropic in that meridian. Correction for other sorts of astigmatism and for astigmatism combined with myopia and hypermetropia can readily be devised by the reader.

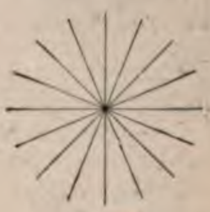

FIG. 220.

D. THE ANGLE BETWEEN THE LINE OF VISION AND THE VISUAL AXIS

The laws of refraction thus far discussed proceed on the assumption that the line of vision coincides with the optical axis of the eye. But this is not the case. The line of vision in front of the eye lies inside of and somewhat above the optical axis, the center of exact vision therefore lying outside of and somewhat below the axis. In Fig. 210 (page 513) $G, G_{\prime\prime}$ marks the line of vision; $F, F_{\prime\prime}$ the optical axis.

The angle between the line of vision and the optical axis is designated as the angle α. Its size in the horizontal meridian is 3.5°–7.0°, and in the vertical approximately 3.5°.

The rays of light entering the eye in the line of vision therefore strike it obliquely. Under these circumstances a homocentric beam remains no longer homocentric, but becomes astigmatic (see page 523), the rays falling in the horizontal meridian being most strongly refracted. This astigmatism however is more than compensated by the ordinary astigmatism of the opposite kind in the cornea.

Assuming the angle α to be 5°, Gullstrand calculated the influence of the oblique incidence of the line of vision for the schematic eye and found that the distance between the two focal lines was only 0.03 mm. and the degree of astigmatism only 0.1 diopter. These figures explain why, as has long been known, the sharpness of vision commonly suffers no reduction from this kind of astigmatism.

E. CHROMATIC ABERRATION IN THE EYE

The refractive index of solid and liquid media is different for rays of different wave length—e. g., that of water for red (spectrum line C) is 1.331705 and for violet (spectrum line G) 1.341285. For a long time it was supposed to be impossible to prevent this dispersion of light into its colors in any optical system. Later, however, it was shown to be possible and instruments have long since been constructed in which no color dispersion at all occurs.

Our everyday experience teaches us that the chromatic aberration in the eye cannot be very great, for in ordinary life it is almost entirely unnoticeable. But more exact investigation of the subject shows that the achromatism of the eye is by no means perfect.

Since the refractive indices of the optical media in the eye for the most part do not differ much from that of water, Helmholtz calculated the dispersion for the reduced eye (see page 512), on the assumption that water was the refractive substance throughout, and found that the posterior focal distance for red (line C) was 20.574 mm. and for violet (line G) 20.14 mm. Actually the color dispersion in the human eye appears to be somewhat greater (the distance between the focal points of red and violet 0.58–0.62 mm. instead of 0.434 mm.). According to Einthoven, the difference in focal distance between the D and F lines in the schematic eye is 0.272 mm.

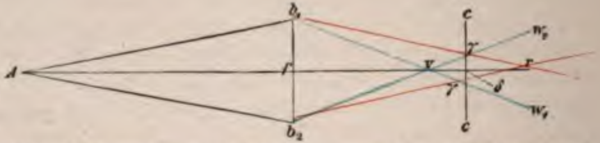

FIG. 221.—Diagram illustrating the chromatic aberration of an eye.

There is, however, a physiological reason as well as a structural one why the color dispersion is not plainly noticeable. When white light enters the eye and the eye adjusts itself for the most strongly effective rays of medium wave length, the latter come together on the retina almost exactly in one point, which is surrounded by a fringe of red and violet rays. But the exciting effect of rays of very great or very small wave length is relatively slight, consequently the action of the fringe zone in comparison with that of the center is negligible. Besides, the center is more strongly illuminated than the fringe zone because rays of all wave lengths strike it.

The same thing is true of the dispersion circles caused by the spherical aberration when the eye is adjusted to the focal point of the central rays.

Only one experiment on color dispersion in the eye can be described here. If one holds before an ordinary petroleum flame a screen with a narrow opening in it and behind this a cobalt-blue glass which shuts out most of the orange, yellow and green rays, but lets through an abundance of ultra-red, indigo-blue and violet rays, the opening may be seen as a luminous point sending out red and violet rays. Now this point appears differently to the observer according to the distance for which the eye is adjusted. If it is adjusted for the red rays, there appears a red spot with a violet halo; if it is adjusted for the violet rays, a violet point with a red halo. This will be evident from Fig. 218 if one imagines the retina in the first case to be located at *r* and in the second at *v*. This experiment is particularly beautiful if an electric incandescent lamp be used.

The colored circles of subjective origin (H. Meyer's rings) which are perceptible around a source of light under certain abnormal circumstances, as in conjunctivitis, or after the effect of osmium vapor, are to be explained by the diffraction of the light about dead epithelial cells, mucous corpuscles, etc., on the surface of the cornea. A similar color phenomenon (Donder's rings) is produced by diffraction at the edges of the lens, but this occurs normally only when the pupil is greatly dilated (Salomonsohn).

F. SUMMARY

Summarizing the optical defects of the eye, we may say that while it exhibits various defects which could not be permitted in a good optical instrument, yet its capacity as an organ of vision is surprisingly little interfered with. The oblique incidence of the line of vision, the difference in the refraction between the different meridians of the cornea, the imperfect correction of spherical and chromatic aberration—none of these nor all of these together diminish the capacity of the eye to such an extent as to produce any perceptible disturbances in vision. But this is true only of the normal eye. It happens not infrequently that these defects exceed the normal limits and then the eye must be described as a rather poor optical instrument. Oftentimes in such cases, the optical properties of the eye can be very considerably improved by practical treatment.

§ 5. THE IRIS

In order that a proper image formed in a camera may not be interfered with by light reflected from the inner walls, the latter are always covered with a dull black color. The *retinal pigment* and the strongly pigmented *choroid coat* serve the same purpose in the eye.

The *iris* which is but the anterior prolongation of the choroid coat likewise has an important function. It has been shown that the laws of refraction in an optical system hold good in case only such rays enter as form a very small angle with the optical axis, and the peripheral rays are shut out. This exclusion of the peripheral rays, so important for the clearness of the images, is provided for by the iris. The pupil can be constricted or dilated by contraction of circular or radial fibers respectively in the iris. Such alterations in the size of the pupil serve the optical requirements of the eye in two ways: in near vision, if this is accompanied by convergence of the optical axes, the pupil constricts and thereby contributes to the sharpness of the image; again, when the asymmetry of the cornea is great, the resulting astigmatism is counteracted to a certain extent by constriction of the pupil. The pupil has in addition the important function of protecting the retina from too intense a light; it constricts in strong light and dilates in weak light.

Constriction of the pupil is caused by contraction of a circular muscle, composed in most animals of smooth muscle fibers and known as the sphincter of the pupil; *dilatation*, by smooth radial fibers known collectively as the dilator of the pupil. The existence of an independent dilator was conclusively proved several years ago by the physiological experiments of Langley and Anderson; it has recently been demonstrated anatomically as well.

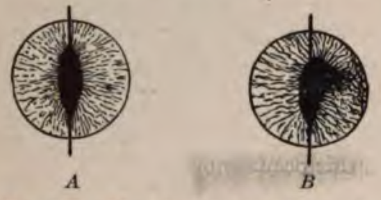

FIG. 222.—The iris of a cat. *A*, at rest; *B*, on stimulating it at the upper right-hand side (Langley).

The muscles of the iris receive their *nerves* by both cerebral and sympathetic pathways. The constrictor fibers are found in the oculo motor. From this nerve they pass over to the ciliary ganglion, connect there with nerve cells (Langendorff), and continue thence through the short ciliary nerves to the sphincter pupillæ. Stimulation of a single one of the short ciliary nerves causes only partial contraction of the sphincter, so that the pupil takes an irregular form. It is stated that the oculo motor at the same time inhibits the dilator of the pupil.

The dilator fibers of the pupil come from the sympathetic. They pass out of the spinal cord by the anterior roots of the seventh to the eighth cervical and the first to the second thoracic spinal nerves, go to the first thoracic ganglion, then through the anterior arm of the annulus of Vieussens to the inferior cervical ganglion, and from this by way of the trunk of the cervical sympathetic to the superior cervical ganglion. From the superior cervical ganglion, the fibers pass to the Gasserian ganglion, follow the trigeminal and traverse the long ciliary nerves, without connecting with the ciliary ganglion, to the iris. Stimulation of the sympathetic is said to cause inhibition of the sphincter as well as excitation of the dilator (Reid).

Both constrictor and dilator fibers of the pupil are in a state of tonic excitation: when the cervical sympathetic is cut, the pupil constricts; when the oculo motor is cut, it dilates.

The following experiments by Langley and Anderson show that the dilatation of the pupil is not merely a matter of inhibition on the part of the sphincter pupillæ. When the sclerotic was stimulated locally with the induction current, a short local dilatation of the pupil (Fig. 222) was obtained. Were the dilatation due solely to inhibition of the sphincter, the movement would have been uniform all around the pupil. Again, when a sector of the iris is isolated except at its ciliary attachment by two radial cuts (Fig. 223), this sector shortens both on direct stimulation and on stimulation of the cervical sympathetic.

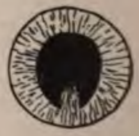

FIG. 223.—After Langley.

Changes in the diameter of the pupil under normal circumstances are for the most part produced reflexly. The most important of these reflexes is mediated by the optic nerve. Constriction begins within 0.4–0.5 second and reaches its maximum in about 0.1 second thereafter (Listing). It requires but an instantaneous flash of light to call out the reflex constriction (v. Vintschgau).

In all animals in which only part of the optic nerve fibers cross at the chiasm (man, monkey, predatory animals and some rodents) contraction of both pupils results—i. e., the reflex excitation passes over from one optic nerve to both oculo motor nerves when light enters but one eye.

Stimulation of other afferent nerves, and powerful respiratory movements, as in dyspnœa, etc., are as a rule accompanied by dilatation of the pupil, although reflex constriction has also been observed with such stimulation. Likewise stimulation of the most widely different parts of the brain, cerebral cortex (motor zone and temporal convolutions), corpora striata, optic thalami, anterior and posterior corpora quadrigemina, produces dilatation. Dilatation of the pupil on stimulation of afferent nerves as well as on stimulation of these various parts of the brain in many cases persists after bilateral section of both the cervical sympathetic and the trigeminal nerves. It must be regarded therefore as, in part at least, the result of inhibition of the constrictor center.

The *tonus* of the constrictor nerves is mainly of reflex origin, for after section of the optic nerve section of the oculo motor no longer produces dilatation of the pupil (Knoll). But stimulation of the optic nerve cannot be the only cause of the sphincter tonus, for the pupil is strongly constricted in sleep.

The *center* for the *constrictor* nerves of the pupil is to be sought in the nucleus of the oculo motor nerve. According to Hensen and Völckers, in the dog it lies in the floor of the third ventricle close to the aqueduct of Sylvius and a little posterior to the center for accommodation (Fig. 230).

The *center* for the *dilatation* of the pupil was located by Budge in the cervical cord (centrum cilio spinale); other authors have been led by their investigations to conclude that the center is located in the brain and that fibers pass thence down the cord to the roots of exit. Since, however, after section of the cord high in the neck, the pupil is dilated on stimulation of the sciatic nerve, but is always constricted by section of the cervical cord alone, we may perhaps safely infer that there is a center in the cord, the normal tonic influence of which is to keep the pupil dilated.

§ 6. ACCOMMODATION

A. RANGE OF ACCOMMODATION

A point of light starting from the far point of the eye and brought gradually nearer to it, can be kept constantly focused on the retina. But this is possible only up to a certain limit, there being for every eye a *near* point whence it receives the most divergent rays which can be focused on the retina. In order that these most divergent rays may be focused on the retina the refraction of the eye must be increased in some way. The change in the eye by which this is accomplished is called *accommodation*. Knowing the far point and the near point of the eye, it is very easy to calculate how much the refraction is increased by accommodation.

The focal distance of the lens which will give to the rays proceeding from the near point the direction they would have if they came from the far point furnishes the measure of the *range of accommodation*.

We have here to distinguish between *range* of accommodation and *line* of accommodation. The former, as just stated, is the measure of the increase in refracting power which can be brought about by accommodation, whereas the latter gives that depth of space within which the eye can form by the help of accommodation a clear picture on the retina. The range of accommodation is entirely independent of the static refraction of the eye; but the line of accommodation varies considerably in eyes of different refractive conditions.

The range of accommodation decreases gradually with age, as the following table compiled by Donders will show:

AGE IN YEARS.	Range of accommodation, Diopters.	AGE IN YEARS.	Range of accommodation, Diopters.
10	14.0	45...............	3.5
15	12.0	50...............	2.5
20	10.0	55...............	1.75
25	8.5	60...............	1.0
30	7.0	65...............	0.75
35	5.5	70...............	0.25
40	4.5	75...............	0.0

This gradual diminution in the optical power of the eye is called *presbyopia*. It must not be confused with hypermetropia, for hypermetropia is a particular kind of static refraction, while presbyopia is caused by a loss in the power of accommodation.

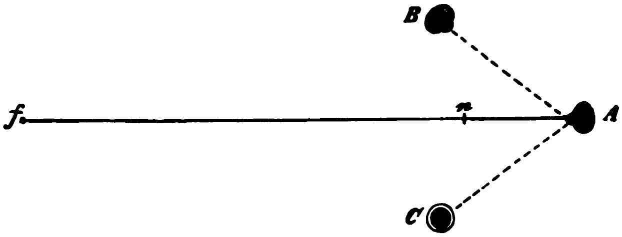

FIG. 224.—After Helmholtz.

Presbyopia is treated with convex lenses, the strength being so chosen that rays proceeding from a point lying conveniently near the eye appear to come from the actual near point. Objects can then be held at any distance and be clearly focused on the retina.

B. MECHANISM OF ACCOMMODATION

The change in the optical apparatus which takes place in accommodation consists in an alteration of the form of the lens. This view was first expressed by Descartes (1637), but the first conclusive proof of it was furnished more than two hundred years later by Max Langenbeck, Cramer, and Helmholtz (1849–1854).

We have already seen (page 522) that the radius of curvature of a spherical refracting surface can be calculated from the size of an image reflected from it. Now it has been shown that in accommodation for near vision the image reflected from the cornea does not change, while that from the anterior surface of the lens, and to a less extent also that from the posterior surface, does. That is to say, the two surfaces of the lens become bulged out more in accommodation, the anterior however to a much greater extent than the posterior.

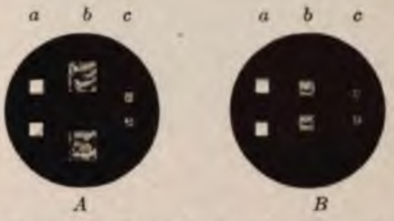

FIG. 225.—The reflected image from the cornea (to the left), that from the anterior surface of the lens (middle picture), and that from the posterior surface (to the right), after Helmholtz. *A*, as seen in an eye adjusted for distant vision; *B*, as seen in an eye accommodated for near vision.

In order to observe these changes of form, the eye to be examined is given two definite points to look at (*f* and *n*, Fig. 224), lying in the same straight line directly in front of it. Then two slits of light from a large bright lamp flame situated to one side of the line of vision and on the same level with the eye are thrown into the eye. In Fig. 224 let *A* be the observed eye and *C* the flame, *B* the eye of the observer. If now the observer move his eye back and forth in the neighborhood of *B*, so that the angle *B A f* is approximately equal to *C A f*, he should see three pairs of images reflected from the observed eye, namely, *a* (Fig. 225), the brightest coming from the cornea, and *b* and *c* from the anterior and posterior surfaces of the lens. When the eye is adjusted for distant vision the images have the appearance of Fig. 225, *A*; for near vision (Fig. 225, *B*), the image *a* does not change, but the image *b* becomes very much smaller. By very exact methods it can be shown also that *c* becomes slightly smaller.

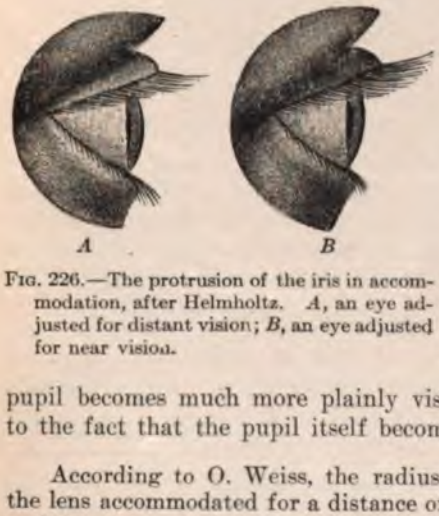

FIG. 226.—The protrusion of the iris in accommodation, after Helmholtz. *A*, an eye adjusted for distant vision; *B*, an eye adjusted for near vision.

With these changes in the form of the lens the pressure in the anterior chamber of the eye does not increase, neither does the posterior surface of the lens change its position, hence the lens as a whole is not displaced. But the anterior surface of the lens presses forward and pushes the iris before it. This can be seen by looking at the cornea of the eye of another person from the side and a little to the rear (Fig. 226). With the observed eye adjusted for distant vision, the observer should place himself so that he can see just a little of the black pupil projecting in front of the sclerotic. Then when the eye is accommodated for near vision, the pupil becomes much more plainly visible. We have already called attention to the fact that the pupil itself becomes narrower in accommodation.

According to O. Weiss, the radius of curvature of the anterior surface of the lens accommodated for a distance of 749 mm., is 9 mm.; for 337 mm., 8 mm.; and for 199 mm., 7 mm.

The whole anatomical structure of the eye indicates that the *ciliary muscle* must in some way participate in bringing about the change in the curvature of the lens. But views differ considerably as to the way in which this takes place.

In a meridional section of the eye, the *ciliary muscle* (Fig. 227) fills up a triangular field in the ciliary body. It constitutes therefore in the whole circumference of the eyeball a circular three-sided, prismatic band, which, as the figure shows, is often interlaced with strands of connective tissue. Iwanoff distinguishes three kinds of muscular fibers according to their direction, namely, (1) meridional fibers running from the sclerotic fold, (3′, Fig. 227) backward to the boundary of the true choroid coat; (2) radial fibers extending from the lamellæ beneath Schlemm's canal to the whole inner face of the triangle; and (3) the circular fibers, the strongest bundles of which run along the short anterior face of the triangle and in its inner anterior angle (15, Fig. 227). Besides, all the radial bundles bend around on the inner face of the muscle, taking a circular direction and forming in this way a more or less extensive circular layer.

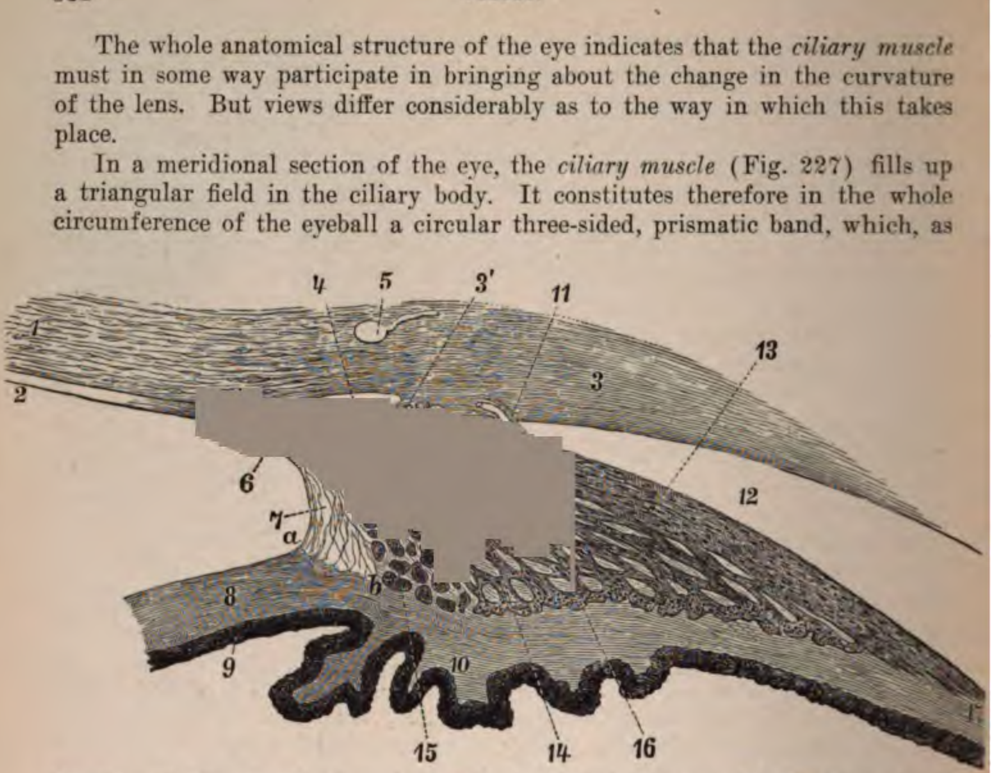

FIG. 227.—Meridional section through the ciliary body of a human eye, after Schwalbe. *1*, cornea; *2*, membrane of Descemet; *3*, sclerotic coat; *4*, Schlemm's canal; *8*, stroma of the iris; *9*, pigment epithelium of the iris; *10*, inner connective-tissue layer of the ciliary body, continuous with the connective-tissue framework of the ciliary process; *13*, meridional fibers of the ciliary muscles; *14*, radial fibers of the ciliary muscle; *15*, circular muscle of Müller; *16*, circular muscle fibers of the inner surface of the ciliary body; *17*, choroid coat.

According to Iwanoff the ring muscle appears to be developed to different degrees in eyes having different static refractive powers; thus in myopic eyes it is almost entirely wanting, while in hypermetropic eyes it is strongly developed and amounts to about one-third of the whole ciliary muscle.

The lens rests in a concavity in the anterior face of the vitreous body and is attached by an anterior prolongation of the hyaloid membrane known as the *zonule of Zinn,* to the ciliary body. The zonule of Zinn surrounds the periphery of the lens, fusing insensibly with its capsule. The greater part of the zonule, from the ora serrata to the tip of the ciliary process, is grown fast to the ciliary body. But, since the ciliary processes do not reach all the way to the lens, there is left a small zone between them and the periphery of the lens, within which the zonule is turned freely toward the posterior chamber. This free part of the zonule (Fig. 228) consists of several strands, which may be divided for convenience into three groups: an anterior, passing to the anterior capsule of the lens and called the suspensory ligament; a middle group whose fibers are directed vertically to the capsule immediately back of the equator of the lens, and a posterior group lying close to the hyaloid membrane and passing over into the posterior capsule of the lens. All these strands consist of parallel inelastic fibers.

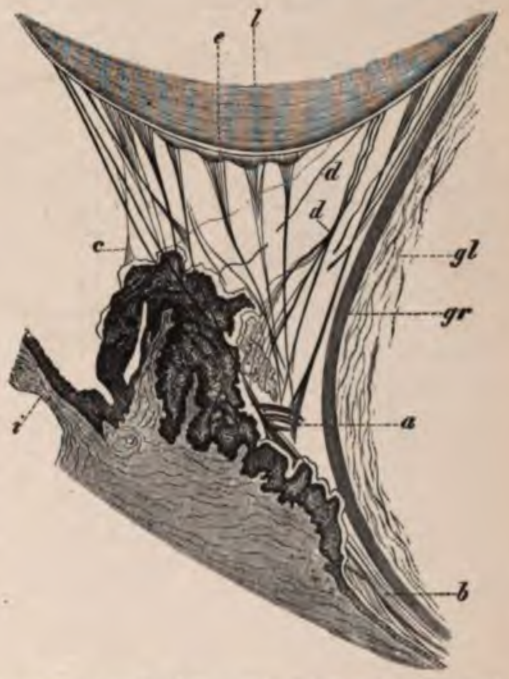

FIG. 228.—Zonule of Zinn of an adult man, meridional section, after G. Retzius. *l*, edge of the lens at its equator; *gl*, vitreous body; *i*, iris; *a*, short, strong attachment fibers of the posterior group; *b*, fibers of the same group springing from the hyaloid membrane; *c*, the anterior group springing from the ciliary process; *d*, fibers springing from the ciliary process and connecting with other fibers; *e*, space between the capsule of the lens and the pericapsular membrane.

Among the hypotheses which have been put forward to explain the form changes of the lens in accommodation, the following by Helmholtz is the one most generally accepted at this time:

The *lens is an elastic body* which, while the ciliary muscle is inactive, is somewhat compressed from before backward by the radial pull of the zonule attached to its equator. Now the zonule is firmly attached by its peripheral or posterior end with the choroid coat just at the posterior margin of the ciliary processes. Consequently by contraction of the meridional fibers of the ciliary muscle (Fig. 227) this posterior edge of the zonule can be drawn forward, thereby releasing the radial tension which it exerts on the lens in the unaccommodated condition. The result is that the lens bulges out at its center rendering both anterior and posterior surfaces more convex. The only function of the circular fibers according to this view would be to crowd the anterior part of the ciliary processes toward the relaxing lens and the zonule, so as to prevent alike any rupture of the tissues and any traction of the anterior part of the zonule which would antagonize the meridional fibers.

Schön seeks to explain the change in the form of the lens in quite another way. In his view the circular fibers, and to a less extent the inner meridional fibers, of the ciliary muscle are the important parts. As a consequence of their contraction the ciliary processes are moved inward and somewhat backward in the direction of the arrow (Fig. 229); the lens, therefore, is pressed upon from all sides and as the schema in Fig. 229 shows, must bulge forward.

Space will not permit us to discuss these different hypotheses more fully. We would merely mention the fact that Hess has brought forward a very weighty argument in favor of the hypothesis of Helmholtz. When the mechanism of accommodation is stimulated by dropping eserin in the eye, the ciliary processes push forward toward the cornea and, at the same time, inward toward the edge of the lens, so that the ciliary processes are then found in front of the equator of the lens. Again, in accommodation for near vision the lens is loose while in the unaccommodated eye it is held firmly in place.

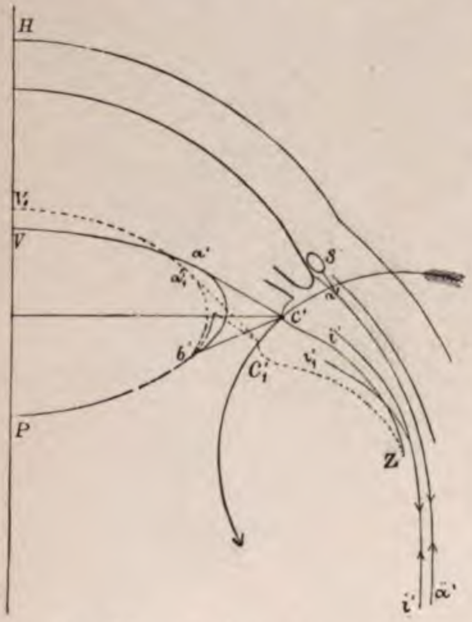

FIG. 229.—Schema of the mechanism of accommodation, after Schön. The form of the lens when the eye is adjusted for near vision is shown by the dotted line.

All authorities agree, that by muscular action the eye can only be adjusted for near vision and not for distant vision.

We have the following statements from Hensen and Völckers with regard to the *innervation of the ciliary muscle.* By stimulation of single ciliary nerves, the choroid is drawn forward, its displacement at the equator of the eye being as much as 0.5 mm.; the anterior surface of the lens bulges forward both in the uninjured eye and after removal of the cornea and iris; and the posterior surface of the lens pushes backward a little.

The fibers innervating the ciliary muscle arise from the oculo motor. From clinical evidence which has recently been gathered by Stuelp it appears that the nuclear center for the ciliary muscle lies close to that of the sphincter pupillæ, and that the *accommodation center* lies in the anterior medial nucleus of the oculo motor, in front of the center for constriction of the pupil. [Fig. 230 represents the modern view as to the location of this center (cf. pages 615, 616).—ED.]

A *convergence* of the optical axes—i. e., a contraction of the internal recti muscles—takes place in accommodation even when one eye is covered. But this association of convergence and accommodation is not an inseparable one, for a person can learn to converge the axes without accommodating, and *vice versa.*

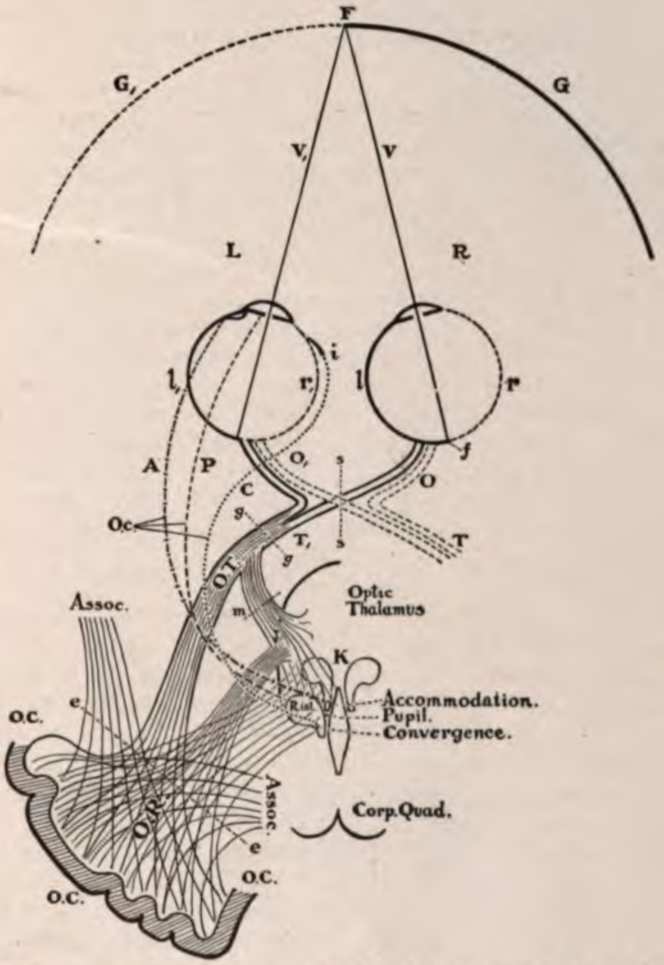

FIG. 230.—Schematic representation of the optic tracts, modified from Fuchs.

The field of vision common to the two eyes is composed of a right half, G, and a left half, $G_{,}$. The former corresponds to the left halves l and $l_{,}$, of the two retinæ, the latter to the right halves r and $r_{,}$. The boundary between the two halves of the retina is formed by the vertical meridian. This passes through the fovea centralis, f, in which the line of vision (V) drawn from the point of fixation, F, impinges upon the retina. The optic nerve fibers arising from the right halves, r and $r_{,}$, of the two retinæ (indicated by the dotted line) all pass into the right optic tract, T, while the fibers belonging to the left halves, l and $l_{,}$, of the two retinæ pass into the left optic tract, $T_{,}$. The fibers of each optic tract for the most part pass to the cortex of the occipital lobe, $O.C.$; the smaller portion of them, m, goes to the oculo motor nucleus, K. This nucleus (cf. page 615) consists of a series of partial nuclei, the most anterior of which sends fibers, P, to the sphincter pupillæ; the next one sends fibers, A, to the muscle of accommodation; and the third sends fibers, C, to the converging muscle (internal rectus, i).

SECOND SECTION

EXCITATION OF THE RETINA AND VISUAL SENSATIONS

§ 1. LIGHT RAYS

Modern physics assumes the existence throughout all space of a rarefied substance, the ether, which, although it has no weight, nevertheless obeys in general the laws which govern the movements of molecules. The density of the ether is so slight that it exercises no noticeable restraint on the movements of the heavenly bodies, with the possible exception of the comets.

Light is regarded as extremely rapid transverse (i. e., vertical to the direction of propagation) vibrations of the ether, which are produced by the luminous point and are propagated through the ether with very great velocity (Huygens, 1678; Euler, Young, Fresnel).

When sunlight enters a dark room through a small slit and then passes through a glass prism, the small bundle of rays spreads out into a broad band, called the *solar spectrum*, which is not now white, as the light originally was, but is of different colors arranged always in the same order: red, orange, yellow, green, blue, indigo, and violet. Sunlight therefore consists of rays which are refracted by the spectrum to different degrees, the red rays being refracted least, the violet rays most.

The difference in refrangibility of these rays is conditioned upon the difference in the rate of their propagation through solid and liquid media. They are also distinguished by different vibration frequencies and consequently by different wave lengths. The wave length (λ) of extreme red rays is 760 millionths of a millimeter ($\mu\mu$), and of the extreme violet rays 397 $\mu\mu$. But the solar spectrum is not limited to that which is visible to human eyes. It contains also rays of greater wave length than 760 $\mu\mu$ (ultra-red rays) and rays of less wave length than 397 $\mu\mu$ (ultra-violet rays). The former are characterized especially by their thermal effects; the latter by their chemical effects on certain silver salts.

The *ultra-red* rays are not visible because, although they are transmitted through the media of the eye, they do not stimulate the retina; while the *ultra-violet* rays are invisible for just the opposite reason—they are for the most part absorbed by the media of the eye. When, as in the operation for cataract, the lens is removed, the visible spectrum reaches down to λ 313.

Different sources of light contain the different rays in different quantity—e. g., the strontium light is red, the sodium light yellow. Accordingly, when the light from such a flame is refracted by a prism we get, not a continuous spectrum, but a spectrum which consists of more or less numerous distinct luminous lines which are characteristic for the different chemical elements.

The color of bodies which are not self-luminous depends upon the rays which are reflected in greatest number from them, or, if the objects are transparent, upon the rays which are transmitted by them. If, for example, a surface is red, it is due to the fact that of all the rays which fall on that surface, the red rays are thrown off in greatest number. Likewise a glass is red because it permits more of the red rays than of any other kind to pass through it. We must remember, however, that it is only the relative number of rays reflected or transmitted which gives the color to a nonluminous object; for rays of other colors may as a rule be reflected or transmitted at the same time.

If all the light rays which fall upon a surface are reflected in the same relative numbers as they occur in colorless light the surface appears white, gray or black according as the total quantity of rays reflected is great or small. The same holds *mutatis mutandis* for transparent objects.

Whether a surface is colored or not its brightness depends upon the quantity of reflected rays: a bright red surface reflects much light of which a relatively large number of the rays are red; a dark red surface reflects the same rays in relatively largest number, but the total quantity of light reflected by it is relatively small.

Two inferences which may be drawn from the facts presented here should be kept steadily in view throughout the following discussion: that white light always consists of rays of different wave lengths and that the only really pure colors are the colors of a pure spectrum.

§ 2. THE PHENOMENA OF EXCITATION

When light falls upon a freshly exposed retina, the latter undergoes a number of changes which are objectively demonstrable. Thus a pigment, present in all parts of the retina except the yellow spot and called because of its color the *visual purple*, fades (Fig. 231); the *coloring matter* of the pigment epithelium (frog's eye, Fig. 232) moves inward, being accompanied in this movement by a shifting of the cone cells in the same direction, and the *action current* of the retina (directed from the inner surface toward the rods and cones) undergoes a positive variation. The significance of the first of these changes we shall discuss briefly on page 541; of that of the second we know little more than what is contained in the statement that it furnishes us some external indication of an excitation process; the third goes perhaps a step farther and brings the mode of response of the visual apparatus into line with other forms of protoplasmic activity. But if we wish to know the course of the excitation process we must rely for the most part on our own *subjective* experiences.

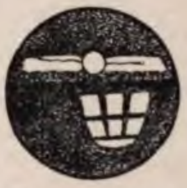

FIG. 231.—Optogram formed on the retina by action of light on the visual purple, after Kühne. The purple fades and the image thus formed is fixed in a solution of alum, after the manner of fixing the image on a photographic plate.

To how great an extent these subjective phenomena are caused by processes going on in the retina itself, or by changes in the many other parts of the nervous system necessary for the production of a conscious visual sensation, nothing definite can be said (except with regard to certain details). Unless otherwise expressly stated the facts and discussion in what follows relate to the entire nervous mechanism concerned in visual sensation.

When light falls upon the retina the resulting sensation does not reach its full strength immediately, and similarly *vice versa* when light is suddenly turned off the sensation does not vanish instantly, but persists for a measurable time.

The latter statement is very easily proved. When one looks for a moment at a bright lamp flame, then suddenly closes the eyes and covers them with the hand, or looks at an absolutely dark background, he still sees a bright image of the same form as that of the bright object itself. The image gradually disappears and as it does so changes its color. This phenomenon in which the bright parts of the object remain bright and the dark parts dark is called a *positive after-image.* Such an after-image has at first the proper color of the object, and very often it reproduces very exactly the separate parts of the object in their proper form and shade.

Proof that the rise of a visual sensation also requires a certain time is not much more difficult. We need only consider for a moment the effect of rotating a circular disk composed of black and white sectors (as in Fig. 233) to be convinced of this. So long as the rate of rotation is low, the black and white sectors remain perfectly distinct. But as the rate becomes higher the edges of the sectors are obliterated, and this is true as well of the edges going before as of those coming after, whichever the direction of rotation. If the excitation of the retina were instantaneous, the leading edges of the white sectors ought to continue sharply defined, while from what has just been said above, it is evident that the edges coming after ought to be indistinct (cf. the dotted line in Fig. 234).

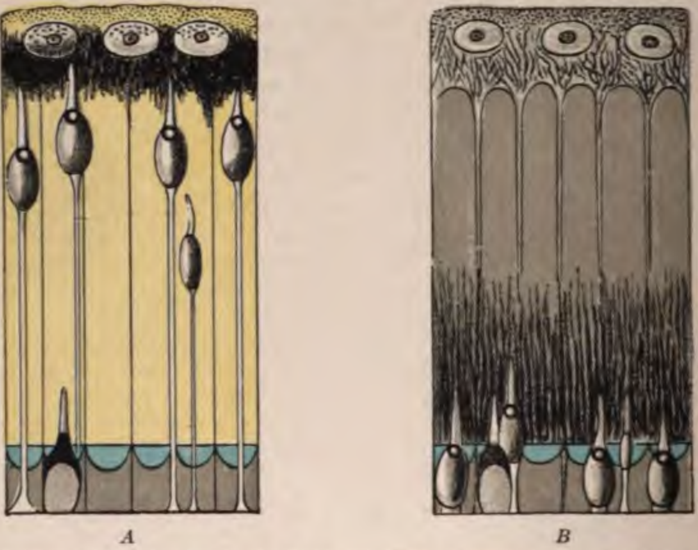

FIG. 232.—Section through the retina of a frog's eye, after Engelmann. *A*, after the eye was kept for from one to two days in complete darkness; *B*, kept for 24 hours in the dark, then exposed for one-half hour to diffuse bright daylight (cf. page 537).

With a high rate of speed the rays coming from the white sectors no longer have sufficient time to produce the maximum excitation and on the other hand the light is never completely shut out by the black sectors; consequently the brightness of the black and white sectors oscillate around a mean value. From a certain rate of rotation onward the whole disk appears uniformly gray, its brightness being the same as would be obtained if all the light reflected by the white sectors were distributed uniformly over the whole disk.

Or in the form of a theorem, when a point on the retina is affected in regular periodic succession for a certain time a by rays of a certain intensity, and is entirely unaffected for a certain time b, if the entire period $a + b$ is short enough, the sensation produced will be a perfectly continuous one and of a strength which (within certain limits at least) corresponds to that obtained by continuous stimulation with light rays of an intensity $\frac{a}{a+b}$ (Talbot's proposition). With light of medium intensity the period $a + b$ need not be less than 0.04 second.

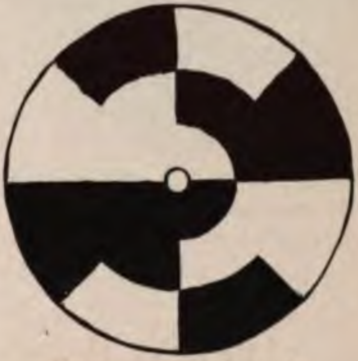

FIG. 233.—After Helmholtz.

The time required to reach the maximum excitation of the stimulus, whatever the interval, is but a fractional part of a second—e. g., as shown graphically in Fig. 235, about 0.217 second. Beyond the maximal point, as is evident from the figure, the excitation gradually declines in intensity owing to the onset of fatigue.

The time required to produce the maximal excitation is different for the different pure colors, being least for the red and greatest for the green (Kunkel). Likewise the time required for the retinal excitation to wear off is different for the different colors.

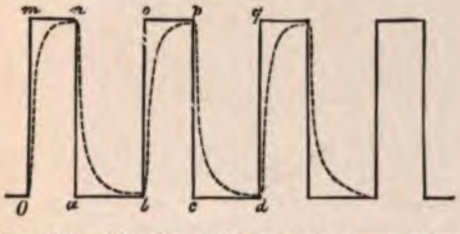

FIG. 234.—Schema to illustrate the course of excitation of the retina successively by black and white sectors (as in Fig. 233), after Fick. If m–n, o–p, etc., represent the white sectors, and a–b, c–d, etc., the black, then the progress of excitation is indicated by the broken line. Starting at O, the retina having just been exposed to darkness, the excitation rises suddenly at first then more slowly: at n the excitation ceases suddenly, but requires some time to fall to the zero point, and so on. The more rapid the rotation, the more will the broken line tend to become a horizontal line.

A. FATIGUE AND RECOVERY OF THE VISUAL ORGAN

When one looks fixedly for a time (with a light of moderate intensity, five to fifteen seconds), at a bright object, and then directs the gaze at a uniformly illuminated surface, he perceives on the latter an after-image, in which the bright parts of the object appear dark and the dark parts bright. That is, the image is just the reverse of what we have called a positive after-image and is described as a *negative after-image*.

This phenomenon is due to fatigue of some part of the visual organ, in all probability of the retina itself. The bright light falling continuously on a certain point of the retina, fatigues that point, so that when light from the uniformly illuminated surface now strikes the retina, that particular point is incapable of being excited so strongly, as the remaining relatively unfatigued parts; hence, the corresponding point of the field of vision appears dark in comparison with the other parts.

In fact the sensitiveness of the retina is all the time changing whether it is being acted upon by the light or is protected from the light—in the one case becoming progressively less and in the other progressively greater. These changes taken together are described by Aubert as the *adaptation* of the retina.

For example, when we pass from a light room into one very feebly lighted at first we are unable to see anything; gradually, however, the sensitiveness of the retina becomes greater, until the feeble light produces a plainly perceptible impression; in fact after remaining longer in the dark room the light can be greatly reduced in intensity without passing below the threshold.

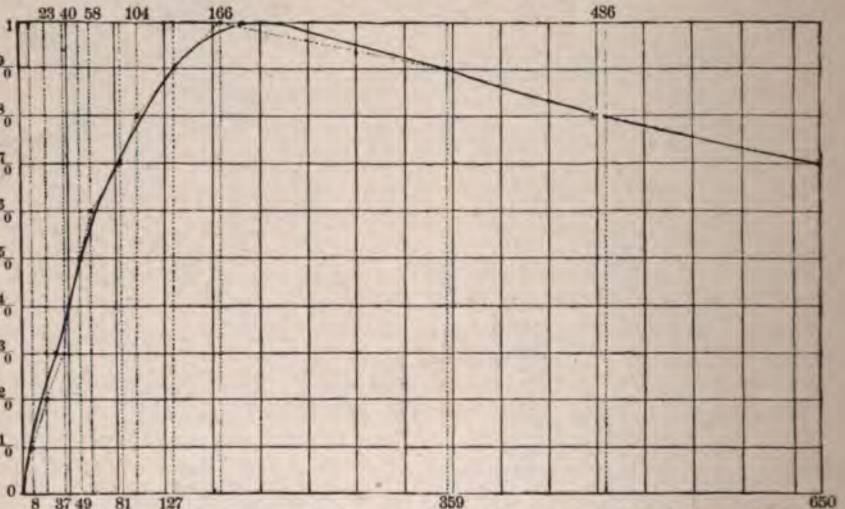

FIG. 235.—Excitation of the retina as a function of the time exposed, after Exner. The abscissæ represent the time in thousandths of a second, the ordinates the strength of the sensations.

According to exact measurements on the adaptation of eyes to the dark the rate is about the same for different individuals, but the absolute increase in sensitivity varies all the way from 1,400 to 8,000 fold. With both eyes the increase in sensitivity is 1.6–1.7 times as great as with only one eye. These facts apply only to the peripheral parts of the retina; for the fovea centralis the adaptation is very much less complete, the increase in sensitivity being only twenty to thirty times the sensitivity of the eye adapted for light.

When we pass back after complete adaptation to the dark into a brightly illuminated room, the strong light at first has a blinding effect upon the retina, which has meantime become extremely sensitive. But, after a short time, its sensitiveness has so far decreased that there is no excessive stimulation. In other words, the eye adapted to the dark has now become adapted to a high degree of illumination. Another point of evidence that the condition of the retina is adapted to the strength of the light, is the fact that the size of the pupil remains the same for a rather wide range of intensity, changing only at the moment the intensity changes.

§ 3. SENSATIONS OF COLOR

There are three different modifications of light which influence our sensations of color: *brightness*, which depends upon the energy of the ether vibrations; *tone*, which depends upon the wave length; and *saturation*, which depends upon the purity of a given wave length, or, in other words, upon the amount of white light present.

The human eye can distinguish all of these properties. Indeed, its ability to distinguish differences of color is very highly developed. König has estimated that in the visible spectrum there are 165 different color tones, which can be distinguished, and that the total number of different degrees of intensity perceptible to the human eye is about 660. When we remember that each tone can vary greatly in intensity and each tone and intensity in turn can have all possible degrees of saturation, we get some idea of the number of possible color sensations.

According to Herschel the mosaic workers in the Vatican can distinguish 30,000 different colors.

A. RELATION OF THE PROPERTIES OF LIGHT TO DIFFERENT CONSTITUENTS OF THE RETINA

Some color tones of the spectrum always appear brighter than others: with light of ordinary intensity the brightest of all is a certain tone of yellow ($535_{\mu\mu}$). If the different colors be observed as the daylight fades it will be noticed that certain ones disappear sooner than others—e. g., the reds before the blues. In a very feeble light a weak spectrum can still be seen, but only as a band of light. Its colors have disappeared and that part of the spectrum which now appears brightest is nearer the more refractive end of the spectrum than it was in broad daylight. But if only a portion of the weak spectrum small enough to be imaged on the fovea centralis be allowed to enter the eye, its color can be correctly perceived (König, Sherman).

These and other facts have led to the assumption of a functional difference between the rods and cones. The *latter*, found everywhere in the retina and exclusively in the fovea centralis, are thought to be sensitive to light of different wave lengths, but to require rather a high degree of illumination. The rods are sensitive to a much feebler light but are not sensitive to color tones (v. Kries, Parinaud *et al.*). Eyes which are totally color blind, remaining sensitive only to light and darkness, are therefore supposed to be devoid of cones. Nocturnal animals like the owl, bat, mouse, cat, etc., are known to have relatively fewer cones and more rods than diurnal animals (Max Schultze).

The *visual purple* (cf. page 537) is also thought to assist in vision by a feeble light. In the first place, it is not found in the cones; and, in the second, there is a close agreement between the brightness of the different wave lengths in a feeble light and their action upon solutions of the visual purple. Accordingly it is conjectured that the fading of the visual purple is of some service in the stimulation of the rods.

B. SUCCESSIVE COLOR INDUCTION

When one looks fixedly for some seconds at a red object on a white ground (Fig. 236), and then turns the eye toward the white ground, he sees on the latter a distinct after-image which reproduces the object exactly in all respects but one—instead of being red it is greenish blue. If the object were greenish blue the after-image would be red.

For every color tone in the spectrum there is another, which in exactly the same way as in this example evokes and in turn is evoked by the first as an after-image. Pure green, however, forms an apparent exception to the rule. Its after-image is purple—but purple is a color which does not occur in the spectrum; its relations thereto will be mentioned presently. Other pairs of colors which are related to each other in this way are: orange and blue, golden yellow and blue, yellow and indigo, etc.

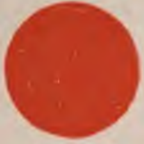

FIG. 236.

These phenomena show that objective light can be subjectively destroyed, also that a certain intimate relation exists between the different colors. In order to inquire further into these facts which necessarily form the foundation stones for every theory of color, we must see what results from the mixture of colors.

C. COLOR MIXTURE

By a mixture of two or more colors we mean that color which is experienced when a given point on the retina is struck simultaneously by rays of different wave lengths. Every color mixture is therefore a summation effect of different light rays.

The best and for many purposes the only possible mode of procedure is to mix pure spectral colors. This may be done by complicated apparatus which enables one to isolate two spectral rays of different wave lengths and to throw them on the same spot of a screen where the mixture can be compared with a reference color.

In this way the different rays are brought into the eye at the same time. But the experiment can be so arranged also that the rays to be tested will fall successively on the same spot of the retina. Then if the sequence is rapid enough a mixture of the two will take place just as in the experiment with white and black sectors (page 539).

Very convenient for this purpose are Maxwell's disks. They are circular, colored disks having a radial slit, so that two or more of them can be overlapped and varying portions of each be exposed to view. If the complex disk thus composed of two or more colored sectors is rotated rapidly by means of a clockwork, the resulting mixture will depend upon the saturation of the individual colors employed and the relative sizes of the different sectors.

The results of color mixture which interest us most are those obtained with the above-mentioned pairs of color—red and greenish blue, yellow and indigo, etc. Experiment has shown that each of these pairs when its components are mixed at a certain relative intensity, produces the sensation of white or gray (which is but a feebly illuminated white). Since each of these colors complements the other, each one furnishing just what the other lacks of being white, they are called *complementary colors.*

The sensation of white therefore can be produced in very different ways, namely, first by the simultaneous action of all the rays contained in sunlight, when they occur in the same proportion as they are there mixed together, and secondly by the proper mixture of two complementary colors. However it is impossible for the eye to tell whether a given white is composed of all the rays of the color spectrum or only of red and greenish blue, orange and blue, etc. White in other words presents only quantitative differences dependent upon different intensities of light, but bearing no relation to the color tones of which it is composed. The eye therefore does not analyze: it lacks entirely the ability so highly developed in the ear, of resolving a given impression into its separate components.

When two colors which are not complementary are mixed together, instead of white we get a new color. If red and violet, the extreme colors of the spectrum, are mixed we get purple, the only color tone which does not occur in the spectrum. Purple is the complementary color of green (see page 542) and is in every way different from the colors the mixture of which produces it.

When two simple colors, separated from each other in the spectrum by less distance than that which separates complementary colors, are mixed, we get a color lying between the two and approaching white more the greater the distance between them, but becoming more nearly saturated the less the distance between the two components. When, on the other hand, two colors separated from each other by a greater distance than that which separates complementary colors are mixed, one obtains purple, or some such color, which lies between one of the components and the corresponding end of the spectrum. In this case the mixture is the more nearly saturated the greater the distance between the components, and approaches white more the less the distance between them (Helmholtz).

	Violet	Indigo	Dark blue	Blue green	Green	Greenish yellow	Yellow
Red	purple	dark rose	light rose	white	light yellow	gold yellow	orange
Orange	dark rose	light rose	white	light yellow	yellow	yellow	
Yellow	light rose	white	light green	light green	greenish yellow		
Greenish yellow	white	light green	light green	green			
Green	light blue	sea blue	blue green				
Blue green	sea blue	sea blue					
Dark blue	indigo						

In the preceding table have been brought together after Helmholtz the results of mixing different spectral colors. At the top of the vertical columns and at the left are found the simple colors; where the vertical and horizontal columns intersect are found the colors resulting from the mixture of the two simple colors standing at the beginning of the intersecting columns.

D. ON THE THEORY OF COLOR

From the facts just given it appears that we can produce the whole series of different color tones by appropriate mixture of a few simple colors. Any physiological theory of color has therefore to show what these simple colors are and to derive all color sensations from them.

There are at this time two principal opposing views as to the production of color, namely, the *three-color theory,* originally proposed by Thomas Young and later developed by Helmholtz, and the theory of *antagonistic colors,* offered by Hering. Since an exhaustive critical discussion of these views would call for entirely too much room and inasmuch as it will probably be a long time yet before the question is finally settled, we shall limit the discussion to a purely dogmatic statement of the essence of the two theories.

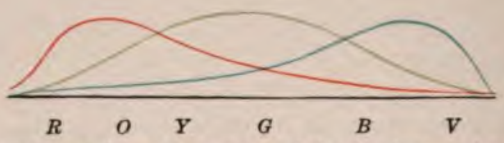

FIG. 237.—Excitation of the different components of the visual organ by light rays of different wave lengths, after Helmholtz.

1. *The Three-color Theory.*—Young regarded *red, green* and *violet* as fundamental or *primary colors*, because they cannot be obtained, at least not in complete saturation, by mixture of other colors. He supposed that in every part of the retina which is capable of all the color sensations, there are three separate nerve elements: stimulation of the first produces the sensation of red; stimulation of the second, that of green; stimulation of the third the sensation of violet. Since the action of light on the percipient parts of the retina is in all probability a chemical process in which certain compounds are broken down, there would be in the retina, according to this theory, three different visual substances corresponding to the three primary colors. In order not to commit ourselves as to the way in which the light acts directly, we shall designate these percipient elements in general as *components* of the visual organ.

Light acts with varying intensity according to its wave lengths, on the three components. The red-perceiving component is excited most powerfully by light of the greatest wave length; the green-perceiving component by light of medium wave length, and the violet-perceiving by light of the shortest wave length. However, it is possible, and for the explanation of certain phenomena it is necessary, to assume that each spectral color stimulates all the components, one of them feebly, the others powerfully.

In Fig. 237 the three curves represent schematically, according to Helmholtz, the relative degree to which each component is stimulated by the different light rays in the production of their appropriate color sensations, thus:

Simple red stimulates the red-perceiving component strongly, the other two feebly; sensations of red.

Simple yellow stimulates the red- and green-perceiving components moderately, the violet feebly; sensation yellow.

Simple green stimulates the green-perceiving substance strongly, the other two much more feebly; sensation green. Other effects can be readily combined from the figure.

Stimulation of all components with about the same intensity gives the sensation of white or of whitish colors.

According to the three-color theory, black is only an extremely feeble white; between the two there is no qualitative difference, but only a quantitative one.

Since according to this scheme the color system of a man with normal vision requires the assumption of three primary colors, the eyes of this class of people are called *trichromatic*.

Starting with the Young-Helmholtz theory König and Dieterici have carried out a very extensive series of measurements and have calculated the form of their (own) curves of sensation for the three primary colors. They found that at the extreme red and the extreme violet ends of the spectrum they could distinguish a difference of brightness, but no difference of color tone, hence these two portions of the spectrum, up to 655 $\mu\mu$ and 430 $\mu\mu$ respectively, must stimulate only the red- and the violet-perceiving components. The results which represent graphically the mean value for the two authors are reproduced in Fig. 238.

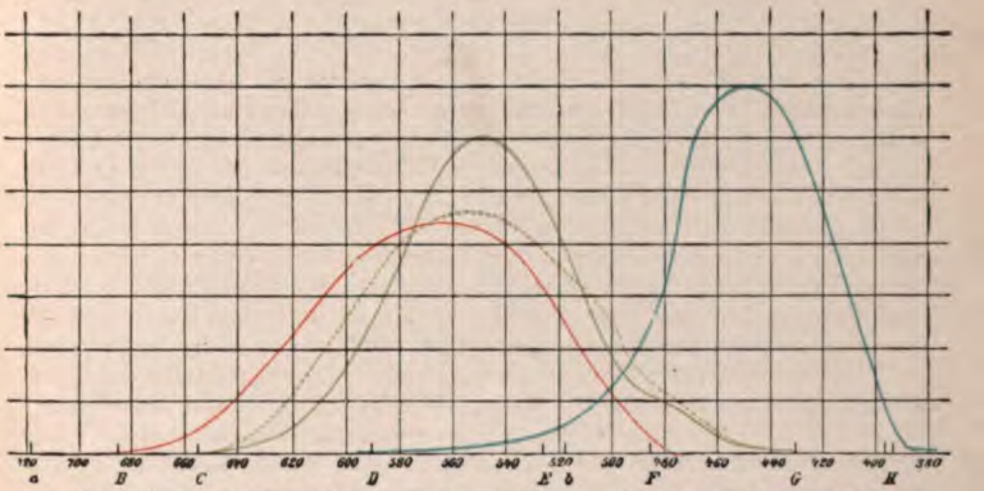

FIG. 238.—Excitation of the different components of the visual organ by light waves of different wave length, after König and Dieterici.

But there are eyes with other color systems, eyes for example for which a mixture of two definite rays, a long- and a short-waved one, can be found to match every homogeneous color. The color system of such eyes is *dichromatic.* This abnormality is as a rule inborn and is spoken of as *color blindness.* If the color system of the normal eye consists of three components, that of the dichromatic eye might be derived from it by the absence of some one constituent. According to the Young-Helmholtz theory there would thus be three possible kinds of color blindness: red blindness, green blindness and violet blindness. From facts which will not be given here it appears that the color systems of the red blind and the green blind do correspond fairly with what would be expected from the theory. Little is known with regard to the third form.

How the color blind actually experience colors can of course only be answered by persons in whom only one eye has been color blind from birth. Hippel and Holmgren have investigated two such cases. It must suffice here to remark that in one of them mixed white light appeared the same—i. e., colorless—to the color-blind as to the normal eye.

In *indirect* or *averted vision* the ability to distinguish colors decreases gradually from the center toward the periphery of the field of vision. The peripheral limits for the different colors, even for a perfectly normal eye, depend upon the intensity of the light, the saturation of the color and the size of the object. Thus Hess found that for a definite shade of red on a gray background, the limit was 20° from the axis of vision, provided the size of the object was 7 mm. in diameter; with a diameter of 30 mm. the same red could be recognized 32° from the axis. According to Landolt, if the intensity of light could be made great enough and the object could be made extensive enough, we would be able to see all colors at the very periphery of the retina.

At all events the capacity for color is much less in the peripheral portions of the retina than in the central portions, and with colored objects of moderate size and moderate intensity of light one may say that a green (of 495 $\mu\mu$) and a red with a moderate admixture of blue disappear entirely at a relatively short angular distance from the line of vision. Yellow and blue can be recognized for some distance farther toward the periphery, in fact all rays of greater wave length than 495 $\mu\mu$ are seen as yellow and all of less wave length as blue. Still farther toward the periphery the sensations of yellow and blue disappear and a zone which is tolerably color blind is reached (Hess).

2. *The Theory of Antagonistic Colors.*—Like the three-color theory, this also proceeds on the assumption that all our visual sensations are conditioned upon the coöperation of a few components (visual substances) in the organ of vision. According to the former theory these are present in the retina itself; but the theory of antagonistic colors leaves it undecided whether these substances occur in the retina, optic nerve or some portion of the brain concerned in vision.

The three-color theory, as we have seen, explains the sensation of white as the result of an equal excitation of the three components and regards white and black as only quantitatively different sensations. According to Hering's theory, black and white are qualitatively different sensations, accompanied by opposite chemical processes in a special black-white-perceiving substance. The sensation of white arises while a process of katabolism is going on in this substance, that of black during a process of anabolism. The brightness or darkness of any purely colorless sensation, accordingly, is determined by the ratio in which the intensity of *katabolism* stands to that of *anabolism*.

Hering assumes four fundamental colors: *red, yellow, green* and *blue*. These colors are selected because they can occur without any tinge of another color occurring with them; or if they do exhibit any evident inclination toward another color, it is never toward more than one other at the same time. For example, yellow can merge into red or into green, but not into blue; blue only into red or green; red only into yellow or blue.

On the other hand, red and green are never clearly discernible in a color at the same time, nor yellow and blue. That is, the presence of an evident red sensation excludes that of an evident green; the presence of blue, that of yellow, and *vice versa*; consequently, Hering calls these mutually exclusive colors *antagonistic* colors.

Just as the sensations of white and black are conditioned upon opposite processes taking place in the white or black substance, the antagonistic colors are produced by anabolism or katabolism, as the case may be, in two other visual substances assumed by Hering, namely, the red-green- and the yellow-blue-perceiving substances. Red and yellow arise by katabolism, green and blue by anabolism.

The main proposition of Hering's theory therefore is this: the fundamental sensations of the visual substances are grouped in three pairs: black and white, yellow and blue, red and green. For each of these three pairs there is a corresponding anabolic and katabolic process of special quality.

Since the amount of anabolism or katabolism caused by a light stimulus in one of the three visual substances depends not only upon the intensity of the stimulus, but also upon the excitability of the visual substance, the same mixture of light may appear bright or dull colored, or colorless, according to the physiological condition of the visual organ.

When the visual organ has been protected from the light long enough so that a condition of balance between the anabolic and the katabolic processes is reached, and a colored light of moderate intensity is then admitted, the excitability for that particular color will decrease until it is less than that for the antagonistic color. Every mixed light which had previously appeared colorless will now be seen with a tint of the antagonistic color, or if before a mixture of fundamental colors was seen, it will now appear as a mixture of the two antagonistic colors. Hering's theory can thus account for the *successive induction* of color or *color contrast*.

Agreeably to his theory, Hering reduces all *color blindness* to red-green and yellow-blue blindness. Those who are blind to red and green lack the red-green visual substance: everything which others see as red or green, they see devoid of color; in all mixed colors containing red or green, they see only the yellow or blue, etc.

E. SIMULTANEOUS CONTRAST

The idea of simultaneous contrast can be most simply presented by means of one or two concrete examples. If small colored sectors be placed on a white disk, as in Fig. 239, and the middle point of each sector be interrupted by a black and white strip, then when the disk is rotated one ought really to see a gray ring, corresponding to the black and white strip, on a faintly colored whitish ground. But instead of looking gray, the ring takes the complementary color of the ground.

Standing in the moonlight and the gaslight at the same time, a person casts two shadows—one from the moonlight, the other from the gaslight. The ground, being illuminated by both the moon and the yellow-red light of the gas flame, takes the color of the latter. The shadow from the moonlight is also yellow red, for it is likewise illuminated by the gaslight. The other shadow which is illuminated by the moonlight ought to be gray, but is not. It has instead a bluish color—i. e., the complementary color of the ground.

Simultaneous contrast therefore means that an object without color, in the neighborhood of a colored one, takes on a tint which is the complement of the color in the object beside which it is placed. In the same way a bright object in the neighborhood of a dark one looks brighter than it really is.

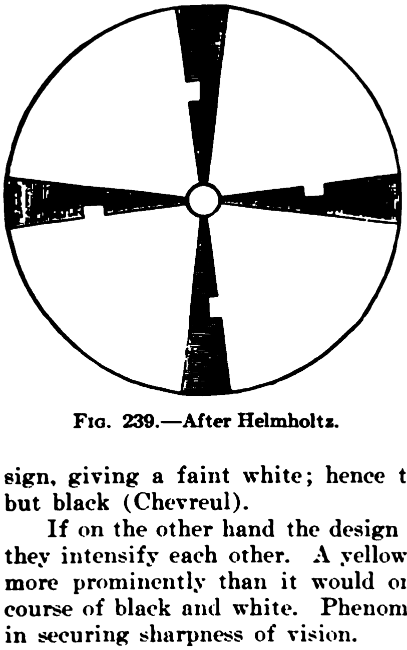
FIG. 239.—After Helmholtz.

We are all the time meeting with contrast phenomena which influence in many ways the impression we get of color compositions. If, for example, a black design be printed on a red material, the design does not appear black, but because of the contrast greenish blue. In order to make the design actually appear black, it is necessary to mix a little of the ground color with the black—i. e., in this case the design must be printed in a very dark red. The greenish blue produced by contrast then mixes with the red of the design, giving a faint white; hence the design no longer appears greenish blue, but black (Chevreul).

If on the other hand the design and ground work are complementary colors, they intensify each other. A yellow design on a blue material stands out much more prominently than it would on any other color; and the same is true of course of black and white. Phenomena of this kind are of no little importance in securing sharpness of vision.

It is evident that these contrast phenomena are entirely of subjective origin and cannot be caused by any objective influence of the one color on another.

According to Helmholtz it is all a matter of judgment. We are accustomed to subtract from all colored surfaces without distinction the light by which they are illuminated, so far as that is in the region of their own color, in order to find the body color itself. If gaslight and moonlight fall on the same spot, the illumination of the ground is a light yellow red. Now this yellow red we abstract not only from the color of the ground, but also from that of the shadow, on which no gaslight falls; hence it looks blue when it is really white.

Hering on the basis of a great variety of experiments makes different objections to this view, and in many cases at least has succeeded in showing that simultaneous contrast is not a delusion of the judgment, but rests upon the *action* of *neighboring spots* in the visual apparatus. The state of excitability of a retinal spot A, for example, is always dependent upon the physiological condition of all the rest of the retina, particularly of the parts adjacent to the spot A. Thus, if the spot A is being constantly stimulated, its excitability may be raised or lowered merely by changing the strength of the light affecting other parts of the retina. Every increase in the intensity of the stimulus on other parts reduces the excitability of the given spot A, so that the sensation mediated by it is less bright. Every decrease in the stimulus on the rest of the retina changes the condition of A so that the corresponding sensation becomes brighter. The same laws apply, according to Hering, to color contrast. That is, if the spot A is exposed to white light and the rest of the retina to yellow-red light, the excitability of the spot A for yellow red is reduced and the white field appears in the complementary color, etc. Hering believes that the effects of adjacent retinal spots on one another play an essential part also in the production of positive and negative after-images.

THIRD SECTION

MOVEMENTS OF THE EYE AND VISUAL PERCEPTIONS

§ 1. ACTION OF THE EYE MUSCLES

In discussing movements of the eye we assume what is only approximately true, namely, that they take place about a definite point called the *center of rotation,* also that when the head is erect and the gaze is directed straight forward the two lines of vision are horizontal and parallel throughout (primary position).

Measurements which have been made to determine the point of origin and the point of insertion of the different muscles, with reference to the center of rotation and the line of vision, as the primary axis, have shown that the three pairs of muscles are not directly antagonistic. The *axis of rotation* of the superior rectus muscle does not coincide with that of the inferior rectus, nor does that of the external rectus coincide with that of the internal, nor that of the superior oblique with that of the inferior. For the sake of simplicity, however, we shall neglect these differences and assume that each pair of muscles rotates the eye about one and the same axis (Volkmann).

The positions of the assumed common axes for the two eyes are shown in Fig. 240. The line *D–D′* is the axis assumed to be common to the superior and inferior recti and *O–O′* that for the two oblique muscles. The axis for the external recti would be vertical to the plane of the paper at *G*. The movement of either eye in the figure caused by the isolated action of each of these muscles may be pictured to oneself by placing the book so that one's own line of vision coincides with the axis of any given muscle, and then imagining the eye in the picture to rotate right or left about the observer's line of vision.

Fig. 241 represents, according to Hering, approximately the paths which the line of vision of the left eye would describe on a plane standing at right angles to the primary axis at the distance *dd* from the center of rotation, if the eye were rotated about the several axes as given in Fig. 240. The position which the horizontal meridian of the eye would have at the conclusion of the movement is shown by a short, heavy line at the end of each path. The length of each path corresponds to a rotation of about 50°; the numbers mark the successive positions of the line of vision.

From this figure it is clear that even if the relations of the axes were in fact as simple as we have supposed them to be, it would be possible to move the line of vision, etc., along a vertical line only by the proper coöperation of at least two muscles. The movement directly upward involves the action of the superior rectus and the inferior oblique; the movement directly downward the action of the inferior rectus and the superior oblique. The former two assist each other in the rotation upward, but the one tends to roll the eye outward and the other inward, so that by a compensatory action the rolling can be prevented altogether. Exactly the same is true of the muscles which rotate the eye downward.

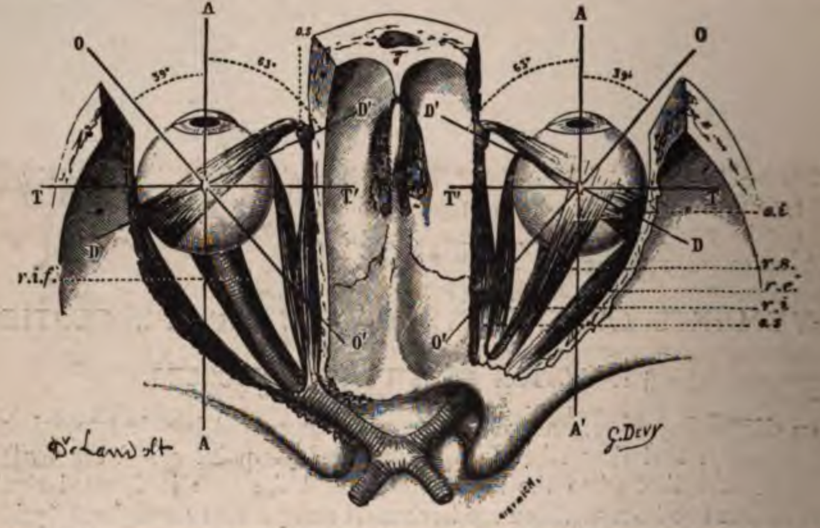

FIG. 240.—The extra-ocular muscles and their axes of rotation, after Fox. The left eye is shown with the superior rectus removed. *r.i.f.*, inferior rectus; *r.s.*, superior rectus; *r.e.*, external rectus; *r.i.*, internal rectus; *o.s.*, superior oblique; *o.i.*, inferior oblique. The line *A A'* represents the line of vision; *T T'*, the transverse axis of the eyeball; *D D'*, the axis of rotation of the superior and inferior rectus muscles: this axis makes an angle of 63° with the line of vision; *O O'*, the axis of rotation of the inferior and superior oblique muscles: this axis makes an angle of 35° with the line of vision. The axis for the internal and external rectus muscles is perpendicular to the plane of the paper at the center of rotation, *C*.

Knowing as we do that the different axes of the eye actually have a less simple arrangement than that here assumed, it is evident, as Volkmann has emphasized, that what are apparently the simplest movements of the eye involve the simultaneous action of several muscles.

A. LIMITS OF THE EYE MOVEMENTS

Helmholtz, Aubert, Hering and others have determined how far the eye can be moved in the different directions by means of its muscles, and have thus mapped out the limits of the field of vision. With parallel lines of vision the monocular fields of the two eyes, projected upon a distant plane, have the positions represented in Fig. 242. The point *m* represents a very distant fixation point. The two monocular fields do not cover each other. The parts accessible only to the left eye are ruled and are designated by the letter *l*, those accessible to the right eye only are horizontally ruled and are designated by the letter *r*.

However it would not be correct to suppose that the unruled part of the monocular field common to the two eyes is in fact the *binocular field*. On the contrary the two lines of vision cannot be directed at the same time to every point in the outer space to which each line of vision can be directed alone. The space surrounded by the line *a a* in Fig. 242 represents the binocular field for distant vision. We see how small is the binocular field common to the two lines of vision; it is much smaller than the field common to both visual axes also for near vision.

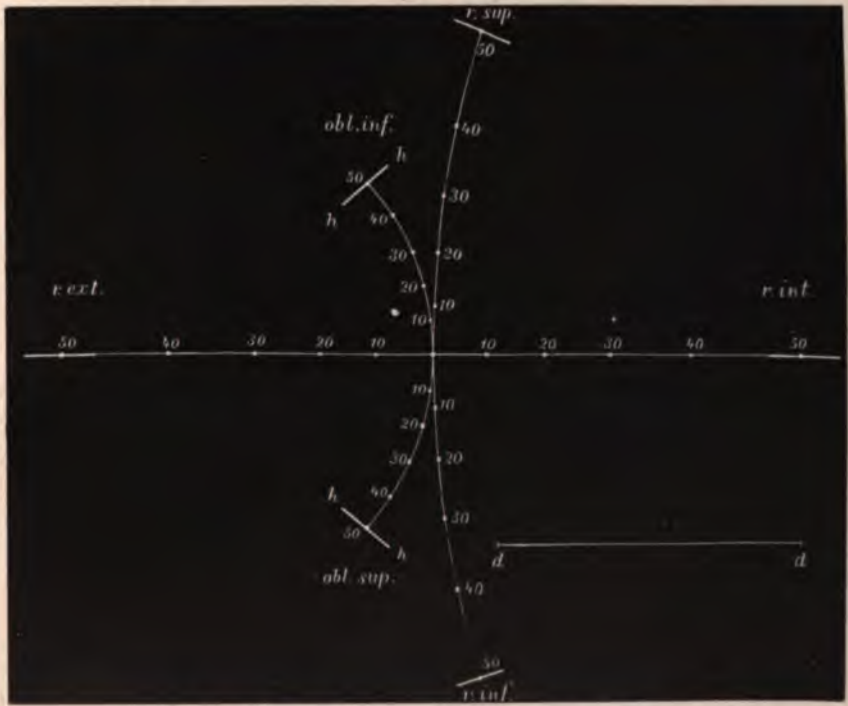

FIG. 241.—The paths described by the line of vision as the result of rotation by the separate eye muscles, after Hering.

The two eyes are very closely associated in their movements. Under normal circumstances the line of vision of the one cannot be directed to a point higher than that to which the other is directed at the same time, and the two cannot be made to diverge.

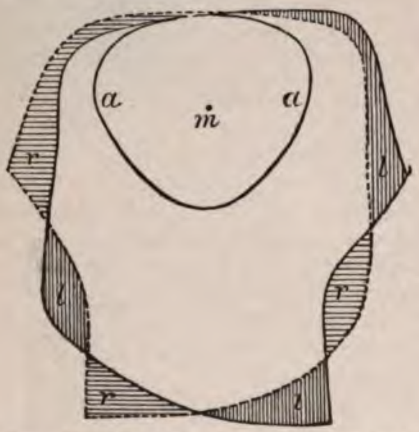

Fig. 242.—The field of vision projected on a distant plane perpendicular to the line of vision, after Hering.

Theoretically, by appropriately combined action of its six muscles, each eye can be turned in any direction and rotated on any axis; but the actual movements are few in comparison with those theoretically possible. In general we may say that only movements with the lines of vision parallel or symmetrically converged—i. e., directed toward a point in the mid line—are possible. Convergence of the lines of vision toward a point not in the mid line is always associated with great effort, and as a rule is obviated by moving the head and thus avoiding, as we are always inclined to do, extreme movements of the eyes.

This limitation of the eye movements is of very great importance for visual perceptions; for the connection between the retinal images and the position of the eyes is thereby rendered more constant than would be the case if all theoretically possible movements were carried out.

§ 2. SIGNIFICANCE OF EYE MOVEMENTS FOR THE OUTWARD PROJECTION OF VISUAL PERCEPTIONS

It is evident from the optical principles of the eye that the images thrown on the retina by refraction of light are always reversed, and yet we always see the objects to which the images correspond right side up. The explanation of this phenomenon has been much discussed, and yet is all very simple.

The newborn child sees, but understands nothing of what it sees. Included in the knowledge which the child gains by experience with the sense of sight is the knowledge of the position of things. But this knowledge the child does not obtain by the sense of sight alone; the bodily movements play a determining part as well. When the child looks at its nurse the image is upside down on the retina. But if it should wish to touch the nurse's head with its hand, it must move its arm in the right direction. In this way a definite connection is established between the retinal image and the movements, and the child learns to project its visual impressions outward in the proper direction.

The reason then why we see all objects right side up is, that in developing our ability to recognize external objects and their position in space, we have always made use of movements of the arm and especially of the eyes themselves, which have taught us the proper direction.

As an illustration of the way visual impressions are projected outward we may take Scheiner's (1619) experiment, which at the same time is an interesting demonstration of accommodation. Two needles are placed one behind the other before a bright background, the one vertical and about 18 cm. from the eye, and the other horizontal and about 60 cm. from the eye. Then a card containing two small holes, whose distance from each other is less than the diameter of the pupil, is held before the eye, and the other eye is closed. If one accommodates now for one needle, while the card is being held so that the line joining the holes is in the same direction as the other needle, this second needle will appear double.

Suppose the eye be adjusted for the distant needle, *b* (Fig. 243, A), then the image of the near needle *a* falls at *a'*. Since each of the two holes admits a beam of light from the near needle, and these two beams cannot fall in the same place on the retina, two faint images are formed at the places where they cross the retina. In the same way by accommodating for the near needle *a* we get a double image of *b* (Fig. 243, B), because the rays from that needle strike the retina at two places. If in the latter case one hole in the card is covered, the image on the same side will disappear; for the image which is formed by crossing (cf. Fig. 230) to the opposite side of the retina has been projected to this side of the field of vision—e. g., the upper image at *a'* in the direction of *b'c*. If, however, the same hole *c* be closed in the first case (Fig. 243, A), the image on the opposite side disappears; the lower image at *b'* is projected not in the direction *c*, but in the direction *d*.

Movements of the eye determine the projection of our visual impressions in other connections also. When one looks through a wire gauze at the window the meshes appear large and far removed from the eye, but if the eyes be focused on a pencil point held close to one's near point of vision in front of the gauze, the meshes appear small and near—i. e., appear in the plane of the fixed point or of the point where the lines of vision meet. Although the experiment gives the same result in looking with one eye, the observer can plainly feel that the eyes are strongly converged in fixing the near object.

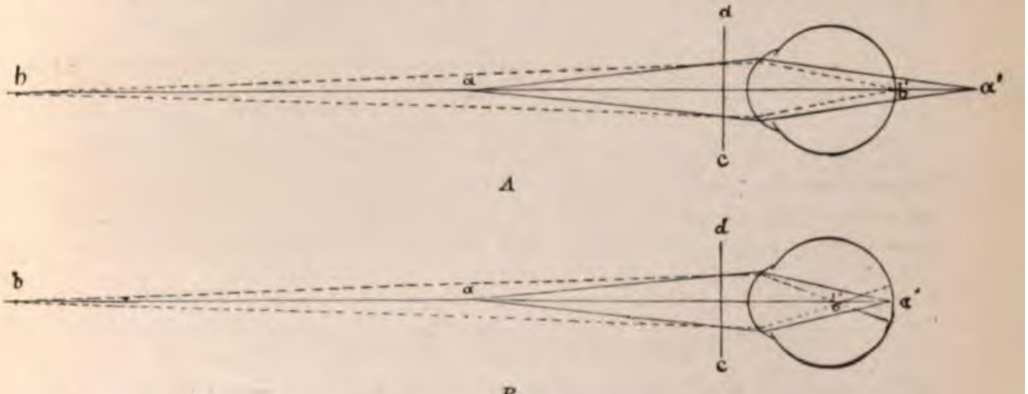

Fig. 243.—Scheiner's experiment.

If, after looking for a moment at the sun until the eye is fatigued, the eyes be turned toward a uniformly lighted wall, one sees there an after-image of the sun, the size of which depends upon the distance of the wall—the farther away the wall the larger the after-image (H. Meyer).

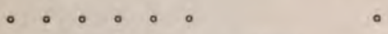

FIG. 244.—After Hering.

We shall return again to the conditions for the perception of depth and the laws by which we judge the apparent distance of an object. From the facts just presented, which are exactly the same with and without accommodation, it follows that a retinal image of a given size is projected in different sizes according to the position of the visual lines, the object appearing smaller when they are converged, larger when they are parallel.

The *size of the retinal image* therefore is not always the determining factor in judging the size of objects. The apparent size of a well-known object—e. g., that of an adult man—does not vary noticeably when it is seen at different distances, although the size of the retinal image changes considerably. Such peculiarities are the result of a gradually acquired experience. A child relying on the size of its retinal images misjudges the size of objects much more than an adult.

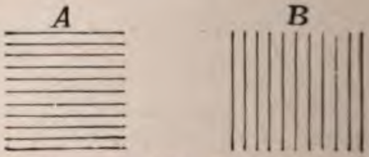

FIG. 245.—After Helmholtz.

In forming judgments of linear, vertical and horizontal distances, equally removed from us, the movements of our eyes play a determining part (Wundt). If we compare a space divided by points or lines into intervals with an equal space not so divided, the former appears greater than the latter (Hering, Fig. 244). Two squares of the same size, one ruled horizontally, the other vertically, appear to be different in both breadth and height (Fig. 245). In both these examples the retinal images of the two objects compared are exactly equal in size, and the accommodation is the same. The basis of the phenomenon appears to be that it requires less muscular effort to cast the eyes over an empty space than over one interrupted at certain intervals. It is as if the eye had to make a fresh effort at each point in Fig. 244, and at each line in Fig. 245.

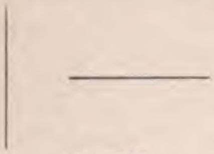

FIG. 246.

The vertical line in Fig. 246 appears longer than the horizontal one because it requires greater muscular effort to move the line of vision up and down than to move it out and in. For in the movement of the visual line directly upward it is necessary that two muscles coöperate (cf. page 550). One of these, the superior rectus, tends to turn the eye upward and inward; the other, the inferior oblique, tends to turn it upward and outward. Hence part of the muscular force developed in each muscle is used in antagonizing the other. But in rotation of the eye directly outward and inward no such compensation is necessary; hence not so much muscular effort is required. The horizontal line therefore *seems* shorter.

§ 3. BINOCULAR VISION

The study of vision with two eyes is of very great interest for physiological psychology, and has been treated by many excellent authorities. Here, however, we must limit ourselves to the most important points and shall only discuss the conditions of single vision and the perception of depth.

A. CORRESPONDENCE OF THE TWO RETINÆ

It is a matter of everyday experience that a distant object regarded with both eyes in their ordinary position looks single, but that if one eye be pushed out of line the object then looks double. One condition of single vision with two eyes, therefore, must be that the images fall on parts of the two retinæ which exactly correspond to each other. Those points of the retinæ upon which the same parts of the two images fall are called *corresponding points*.

On purely optical grounds it is evident that only two points can correspond, for with any given position of the eye a luminous point can be pictured at but one definite spot in each eye. The centers of the two fovæ centrales represent corresponding points. The exact position of others can be determined experimentally by means of an instrument known as the haploscope (Hering). It is evident on reflection that the nasal side of one retina must correspond to the temporal side of the other, since light from, say, the right side of the field of vision must strike the left side of both retinæ and *vice versa.*

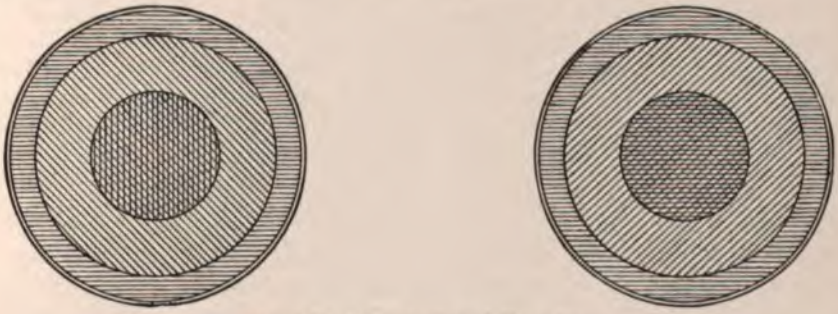

FIG. 247.—The rivalry of the retinæ.

B. SINGLE VISION WITH TWO EYES

It might be supposed in explanation of the remarkable fact of single vision with two eyes, that the optic nerve fibers proceeding from corresponding points of the two retinæ end in the same ganglion cell of the brain. But this is not true, for the independence of each eye is much greater than it would be on this hypothesis. There is a form of squint—i. e., pathological deviation in the positions of the eyes—which is due to an abnormal shortening of the eye muscles (muscular strabism). The line of vision of the squinting eye deviates by a certain angle from the proper position. Now it happens that the person so affected sees single with two eyes in which the images do not fall on symmetrical points. If so, these asymmetrical points would nevertheless be corresponding points. But suppose by a slight operation, the squinting eye be given its proper position; at once double vision results, which though for a time very disturbing, gradually disappears, either because the person learns to disregard one image, or it may be, by a new arrangement of the corresponding points of the two retinæ (Wundt).

If we take two patterns ruled in different directions (as in Fig. 247) and look through cylindrical tubes at one with the left eye and at the other with the right, we should expect, if the corresponding points of the two eyes were connected with the same ganglion cells, to get a double pattern ruled both ways. But instead, when the vertical lines of one pattern are seen clearly, the horizontal lines of the other are indistinct and *vice versa.* If the eyes be moved in the vertical direction, the vertical lines stand out more and more prominently—if in the horizontal direction the horizontal lines.

Because the two fields of vision appear thus to contend for the supremacy, this phenomenon is known as the *rivalry of the retinæ.*

The question whether the correspondence of the retinæ is inborn or acquired has been answered in very different ways. At all events we may be sure that the nerve connections for the movements of the two eyes and for keeping them in their natural positions are established before birth. For this reason the portrayal of an object on certain parts of the retina is especially favored. Since now the bilateral connection of the optic fibers with the cerebrum is, for the most part at least, inborn also, there must exist from the earliest moment of extra-uterine life onward very favorable conditions for the correspondence of the retinæ. Hence it will be relatively easy for the child in the formation of his visual sensations to relate the two retinal images, together with the tactile impressions, to a single object and thus gradually to develop a correspondence of the two retinæ.

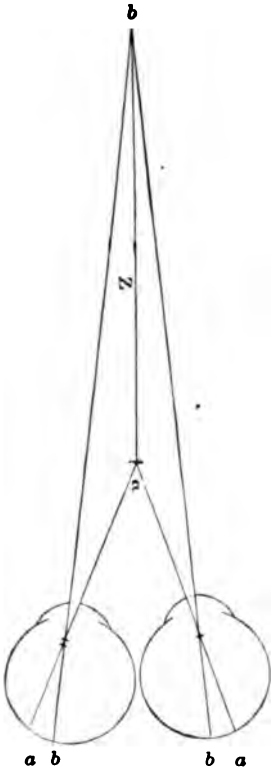

FIG. 248.—Schema illustrating the formation of images in the two eyes, of an oblique line in the median plane.

C. PERCEPTION OF DEPTH

The principal significance of vision with two eyes is that it enables us to estimate distance in the sagittal direction more exactly and to obtain an idea of the solidity of objects.

It is true that one can estimate distances with one eye, but he can do so much more accurately with two.

The factors which figure in the perception of depth *with one eye* are the following: (1) visual angle; (2) accommodation; (3) convergence of the lines of vision.

It is evident that the visual angle can figure only when we are dealing with objects which vary but slightly in size, and which are well known to us. But under these circumstances and especially at great distances where accommodation and convergence can have no part the visual angle is of very great importance.

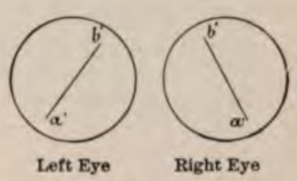

FIG. 249.—The position of the two images (Fig. 248) on the retinæ.

As we have already seen (page 534), accommodation and convergence are very closely connected, and convergence occurs in accommodating for near vision even when one eye is covered. Since accommodation is not necessary for vision with emmetropic eyes at distances in the sagittal direction of more than 5 m., and only becomes of great importance at a much smaller distance, it is evident that these two factors can only figure for relatively slight distances.

If a thread be placed obliquely in the mid line of the body, so that its near end (Fig. 248, *a*) is higher than its farther end (*b*), one can tell even with an instantaneous flash of light from an electric spark—when the eyes have not time to move—the correct position of the thread, and it never appears double (Aubert). And yet, as Fig. 249 shows, the images of the ends of the thread do not fall on corresponding points of the retina, and from what we have already learned we should suppose that the thread would produce an impression of two lines lying in the same plane and crossing each other. By looking very sharply, in fact, one can get such an impression; this means that we have here an ability which is not inborn, but is acquired by practice and experience.

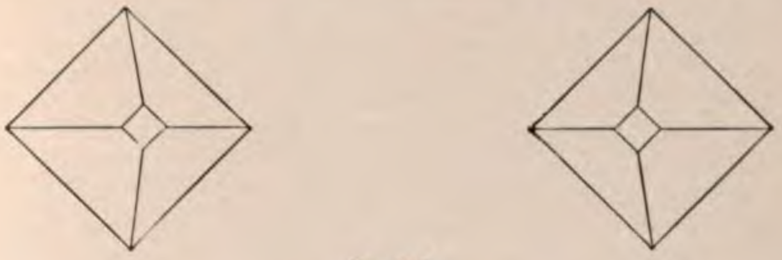

FIG. 250.

It follows from the experiment that the excitation of two dissimilar points of the retina does not always produce a double image, but under some circumstances gives the idea of a single objective point. This point, however, is not in the plane of the fixed point, but lies either in front of or behind it.

The *accuracy* with which we can perceive differences of depth by vision with dissimilar points is exceedingly great. According to Heine, for persons endowed with extraordinary acuteness of vision a displacement of the retinal picture of only 6 seconds of an arc (0.0005 mm.) is perceptible. Thus at a distance of 5 m. a displacement in the sagittal direction of 10 mm. would be perceptible, and at a distance of 100 m. a displacement of 20 m. Individuals with normal acuteness of vision could perceive a displacement of about twice this amount.

The above-mentioned experiment represents *stereoscopic vision* in its simplest form. When we look at a solid object, not too far removed, first with the right eye and then with the left, the picture we get of the object is not exactly the same for the two eyes. The right eye sees a little more of the right side of the object, the left a little more of the left side. In Fig. 250 are represented the images of a truncated pyramid as seen by the two eyes separately. A glance at the two is sufficient to convince one that these two images could not possibly fall on corresponding points of the retinæ. But if these drawings be held before the eyes so that the one may be seen with the right eye and the other with the left, the two fuse together in our minds into a picture of an actual pyramid.

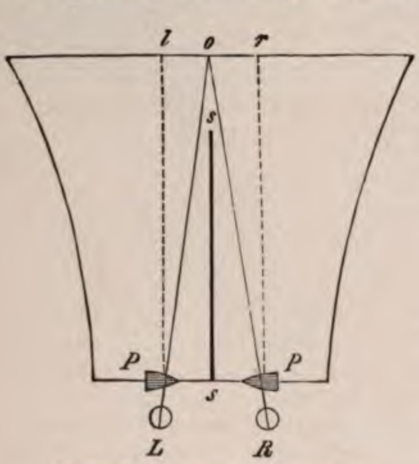

FIG. 251.—Brewster's stereoscope.

Unless one is accustomed to accommodate the eyes without converging the lines of vision this experiment is difficult. The same result is obtained without accommodation if the two pictures be refracted separately into the two eyes by means of lenses. This is the principle of the common stereoscope of which Brewster's form (Fig. 251) may be taken as an example. It is apparent from the figure that two pictures situated at *l* and *r* will be refracted so as to be superimposed at *o*.

For stereoscopic vision to be of any importance the object must not be too far removed, for then the images belonging to the two eyes would not be noticeably different. The ordinary stereoscopic views of landscapes are photographed with a double camera so that the plates are farther apart than the distance between the two eyes. Consequently such photographs combined give us an impression of solidity such as natural vision does not afford.

REFERENCES.—*Aubert*, "Physiologische Optik" (Graefe-Saemisch's "Handbuch der Augenheilkunde," ii, 2, Leipzic, 1876).—*Fick*, *Kühne* and *Hering*, "Gesichtssinn" (Hermann's Handbuch der Physiologie, iii, 1, Leipzic, 1879).—*Helmholtz*, "Handbuch der physiologischen Optik," second edition, Hamburg and Leipzic, 1886–1896. The last named cites a very complete literature of the subject of physiological optics.—*Hering*, "Zur Lehre vom Lichtsinn," Wien, 1878.—*v. Kries*, several articles on the "Physiologie der Gesichtsempfindungen," Leipzic, 1897–1902.—*v. Kries*, *Nagel* and *Schenck*, "Gesichtssinn" (Handbuch der Physiologie, iii, 1, Braunschweig, 1904).—*Wundt*, "Text-book of Physiological Psychology," translated by E. B. Titchner, New York, 1905.

CHAPTER XXII

THE PHYSIOLOGY OF THE NERVE CELL AND OF THE SPINAL CORD

§ 1. GENERAL CONSIDERATIONS CONCERNING THE FINER STRUCTURE OF THE NERVOUS SYSTEM

It has for a long time been customary to divide nerve tissue into two elements: *nerve cells* and *nerve fibers*. The nerve cells were first seen by Ehrenberg (1833) in the spinal ganglia. Remak (1835) first pointed out that the processes of nerve cells are continued in the sympathetic nerves of the vertebrates as an integral part of the nerve fibers. This was shown to be true also for the invertebrates by Helmholtz and Hanover (1842). Deiters (1863) demonstrated that all central nerve cells have two kinds of processes: first, *axis-cylinder processes*, which connect with the medullated nerve fibers and become directly continuous with this axis cylinder; and secondly, *protoplasmic processes*, which break up into very fine branches whose ultimate fate Deiters was unable to ascertain.

By the introduction (1873) of *Golgi's method* of impregnating the nerve elements with silver, a fresh impetus was given to research in the field of neuro-histology. With the application of this method, which has given us such a rich and comprehensive view of the structure of the nervous system, are associated preëminently such names—apart from that of Golgi himself—as those of Cajal, Kölliker, Retzius and von Lenhossek.

According to the view represented by these investigators the nervous system is to be regarded as made up of genetically separate and distinct nervous units to which the general term *neurons* is now applied. The most essential and important part of the neuron is the nerve cell. Several processes are given off from this, one or two of which (from some cells more) are continued as the axis cylinders of nerve fibers and consequently are termed axis-cylinder processes or *axons*. As for the remaining processes, the so-called dendrites or protoplasmic processes of Deiters, they divide into numerous branches which become exceedingly attenuated, and in this way greatly increase the superficies of the nerve cell.

The nerve process continues as an integral part of the nerve fiber to its final distribution, where it generally breaks up into a small terminal arborization. At different points along the course of the nerve fiber a variable number of side twigs or collaterals are usually given off, which, in turn, after a shorter or longer course, like the nerve fibers themselves, end in delicate ramifications.

According to the original conception of the *neuron theory* the individual nerve units do not form a continuous network, but are anatomically separate and distinct, although both in the central and in the sympathetic nervous system the end tree of one neuron may twine about the cell body of the second so that the latter is brought into contact with the former neuron. Any anastomosis or actual structural continuity of dendrite with end arborization is, therefore, emphatically denied. Everything takes place by mere contact.

In view of the work of Apáthy and Bethe, this position, however, is no longer tenable, for it appears to have been definitely shown that the different nerve units do unite by anastomosis.

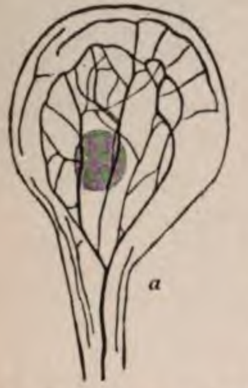

FIG. 252.—Ganglion cell of a leech (*Hirudo*), with fine peripheral network and coarse inner network. From the latter a stout efferent fibril is given off (Bethe).

According to Apáthy's researches—chiefly on invertebrates—the nerve fibers consist of fine neurofibrils which constitute independent morphological elements. Within the nerve fiber they preserve their individuality throughout and have no connection whatever with one another. In the peripheral end organs the individual fibrils split up and form an anastomosing network. Likewise *in the ganglion cells* the fibrils which enter become branched and form a network. But before entering the cells the delicate end twigs of the afferent fibers form a reticulum within the dense tangle known as the *neuropile*, which occupies the center of the ganglion. From this neuropile very delicate fibrils emerge, penetrate the ganglion cells and there form first a peripheral network (Fig. 252), from which are given off in turn radial fibrils that weave about the cell nucleus a second network of thicker fibrils and from this finally the stout efferent fibril emerges. The neurofibrils therefore represent the conducting portion of the nervous system and through them all parts of the nervous system are brought into direct communication with one another (according to Bethe).

In certain invertebrates at least (green crab, crawfish), but a small portion of the neurofibrils pass through the nerve cells. Here, then, the fibrillar transition from fiber to fiber, and their intermixture must take place, for the most part, in the neuropile and its reticulum.

Bethe in particular showed that the neurofibrils are present as conducting elements in the *nervous system of the vertebrates* also. Without any interconnection the fibrils run a separate and unbroken course to the terminal arborizations of both the peripheral nerve fibers and their analogues the medullated fibers of the central nervous system. They occur in the nerve cells also, and almost every cell process is connected with one adjacent to it by a bundle of fibrils of variable thickness. In like manner each dendritic process sends some fibrils into the axis-cylinder process of the cell.

Covering the surface of the nerve cells and of their dendritic process there is found a network with polygonal meshes (Fig. 253), concerning whose real nature different views have been advanced. It was first described by Golgi. According to Bethe, who, however, expresses himself very cautiously in this regard, this network is of a nervous character, connecting on the one hand with the neurofibrils of the nerve cells, and on the other with nerve fibers from without. Accepting this view, this pericellular network would be analogous to the extracellular fibrillary reticulum in the neuropile of the invertebrates. In view of the fact that it is not confined alone to the surface of the cell, but spreads out in three dimensions through the entire gray matter of certain parts of the nervous system, this network may be looked upon as constituting a new kind of nerve matter, probably corresponding to the extracellular "gray" whose existence was postulated by Nissl. Nissl's inference was based on the ground that even the great number of nerve cells, dendritic and axis-cylinder processes, neuroglia fibers and cells, and blood vessels taken collectively, especially in certain parts of the cerebral cortex but also in other places, fall far short of the bulk necessary to fill the entire space.

What the genetic relationship is that exists between the reticulum of the invertebrate ganglion or the Golgi network of the vertebrate nerve tissue—if indeed it be a nervous structure—and the nerve cells is still quite unknown. Even if the pericellular network takes its origin from the nerve cells and is therefore to be regarded as a derivative of such a structure, the classical definition of the *neuron theory* makes no provision or qualification for such an additional element. Moreover, Bethe and others have made observations which purport to show that the nerve fibers are not produced as outgrowths of the nerve cells but are laid down separately by other cells. If this be true, the neuron theory cannot be maintained in any form. But since much remains yet to be cleared up in regard to this question, and since different facts of experimental physiology which Bethe has advanced in support of his view (cf. page 575) really admit of another theoretical construction, the objection last urged against the neuron theory can scarcely yet be accepted as conclusive.

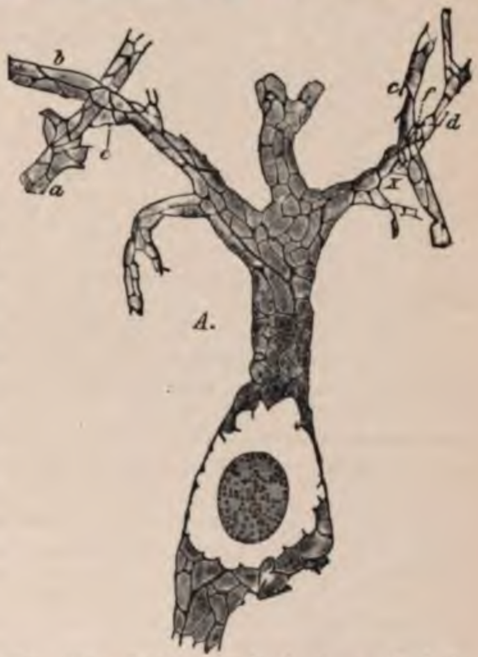

Fig. 253.—Golgi network about a cell of the nucleus dentatus of the dog, after Bethe.

At present we may view the structure of the nervous system somewhat as follows: The nerve cells give off several processes, one or more of which become the axis cylinders of nerve fibers. These consist of fine fibrils which pursue a separate and unconnected course in the nerve fiber, oftentimes penetrate the nerve cell and there—in the invertebrates, but not in the vertebrates—form a real network. These fibrils anastomose freely outside the nerve cells, and also within the cells in the invertebrates, and thus constitute a possible path for the transmission of stimuli from one cell to the other.

It must be observed, however, in this connection, that our knowledge concerning the finest structure of the nervous system, especially in the vertebrates, is still too meager to admit of any one satisfactory or conclusive view.

§ 2. THE STRUCTURE OF THE SPINAL CORD[1]

A cross section of the spinal cord (Fig. 254) shows the central *gray matter* with its contained nerve cells, and surrounding it the *white matter* made up of nerve fibers. The anterior longitudinal or median fissure (*a*) and the posterior median septum (*b*) divide the cord into two symmetrical halves, connected by two commissures (*q*, *r*), the anterior white and the posterior gray commissures.

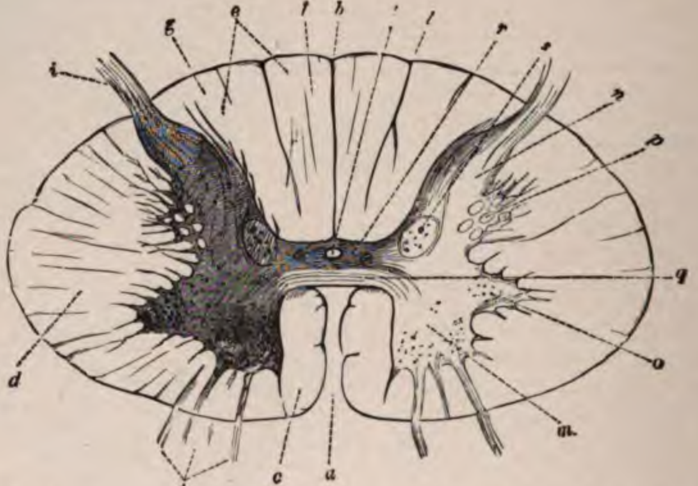

FIG. 254.—Semidiagrammatic section of the spinal cord, after Erb. *a*, anterior fissure; *b*, posterior septum; *c*, anterior column; *d*, lateral column; *e*, posterior column; *f*, funiculus gracilis; *g*, funiculus cuneatus; *h*, anterior root; *i*, posterior root; *k*, central canal; *l*, sulcus intermedius posterior; *m*, cells of the anterior horn; *n*, cells of the posterior horn; *o*, lateral horn; *p*, processus reticularis; *q*, anterior commissure; *r*, posterior commissure; *s*, Clark's column.

The gray matter, pierced in the middle by the central canal (*k*), has in general the appearance of the capital letter H, but varies somewhat in form at different levels. The roots of the nerves enter each half of the cord in separate bundles, the posterior and the anterior spinal nerve roots. These divide the white matter into three main portions: (1) the anterior column lying between the anterior longitudinal fissure and the anterior nerve root; (2) the lateral column lying between the anterior and posterior nerve roots; (3) the posterior column lying between the posterior nerve root and the posterior median septum.

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[1] After Edinger's "Vorlesungen über den Bau der Nervösen Zentralorgane," seventh edition, Leipzic, F. W. C. Vogel, 1904. Since the more recent views, as set forth in the paragraphs above, on the structure of the nervous system are still immature, and fall short of a comprehensive exposition of the structure of the spinal cord, in the account here and in that which follows we shall make use of the anatomical facts thus far established without further reference to the relation and connection which may exist between the individual cells and fibers.

The gray matter on each side of the cord is divided into an anterior and a posterior horn. In the lower cervical and in the upper thoracic regions of the cord, as well as in the lumbar region, the lateral portion of the anterior horn becomes partly separated off as a lateral horn (*o*).

Among the *nerve cells* of the gray matter we distinguish: (1) The cells arranged in groups in the anterior horn; (2) the cells of the so-called column of Clarke (*s*) situated at the median side between the anterior and posterior horns, and extending from the end of the cervical enlargement to the beginning of the lumbar cord; (3) the cells of the substantia gelatinosa Rolandi capping the posterior horn; (4) the rest of the cells in the posterior horn.

The fibers of the anterior nerve roots are the axis-cylinder processes of the cells in the anterior horn of the same side, or, less frequently, of the opposite side, the latter fibers crossing *via* the anterior commissure before they gain the anterior root. The cells of the posterior horn on the contrary do not connect directly with fibers of the posterior root, since the latter have their origin in the cells of the spinal ganglia.

These *cells of the spinal ganglia*, for the most part, are unipolar—i. e., they have but one process which, however, after a short course, splits into two branches. One of the two proceeds toward the periphery and joins the anterior nerve root in a mixed nerve trunk; the other enters the cord by the posterior nerve root. Practically all of the fibers which enter the cord divide into an ascending and a descending branch, both of which give off collaterals, and sooner or later end like the collaterals about the cells of the gray matter of the cord. The peripheral nerve fibers, therefore, have their origin either in the cells of the anterior horn or in the cells of the spinal ganglia.

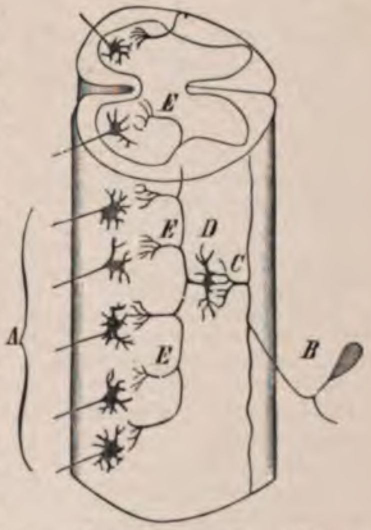

FIG. 255.—Schema, after Kölliker and Lenhossék. *A*, motor cells with root fibers; *B*, spinal ganglion cell with its processes; *C*, a sensory collateral; *D*, column cell with T-shaped branching processes; *E*, collaterals of the same.

The nerve fibers from the anterior horn cells are all *efferent* in function, and the nerve fibers arising from the cells in the spinal ganglia are mainly *afferent* fibers.

With regard to the further connection of the two kinds of fibers we distinguish: (1) a secondary efferent path; (2) a secondary afferent path; and (3) the paths by which afferent pass over into efferent impulses.

Those tracts which connect the nerve cells of the anterior horn with the higher centers we designate as *secondary efferent paths*. They are the paths by which impulses liberated in the cells of the higher centers are conveyed to the motor cells of the anterior horn.

The fibers entering the cord from the spinal ganglia are brought into relation with the cells of the posterior horn whose axis-cylinder processes constitute the *secondary afferent paths*. It is by these paths that impulses are transmitted to the higher centers.

The transition from afferent to efferent paths may occur in several ways. The simplest instance is when an afferent nerve fiber or one of its collaterals connects directly with the motor cell of an efferent nerve fiber or with some of its processes by means of fibrils.

this increase of tonus would be of no use if the point of insertion of these muscles were not fixed, hence there must be also an increase in the tonus of the trunk muscles on the opposite side. The cerebellum exercises this regulating influence by means of the various pathways proceeding from it to the motor nuclei in the spinal cord and to the motor cortex in the cerebrum (cf. Fig. 271).

It is likely that the *compensation* which gradually appears after extensive injury to the cerebellum is the work of the cerebrum, particularly of the motor regions (cf. Chapter XXIV). The following observations by Luciani speak for such an explanation:

Three operations were performed on the same dog: in the first the right half of the cerebellum was removed; in the second the motor regions of the cortex were destroyed in both cerebral hemispheres; and in the third the remainder of the cerebellum was taken away. The animal remained alive for eleven months after the operation and was then killed. During these eleven months he could neither hold himself up nor walk without support. In none of the animals observed by Luciani in which the cerebellum alone was destroyed, did anything like this occur. The difference was due, as Luciani observes, not to the mere extirpation of the cerebral cortex, for this operation of itself produces only transitory symptoms. It appears rather that destruction of the motor cortex removed just those conditions which made it possible for the animal without a cerebellum to find the necessary compensatory movements. It is especially worthy of remark that swimming movements, which do not require to be coördinated so finely as walking movements, could be performed by this animal perfectly well.

The motor disturbances which appear *immediately after the operation* on the cerebellum, the peduncles, or the pons are particularly severe and should be given special mention. The animal sometimes gets into certain attitudes called *forced positions*, which it seems unable to get out of, returning inevitably to the same posture every time it is compelled to take another; or it performs what are called *forced movements*, rolling over and over around the long axis of the body, or running around in a circle like a circus animal, or describing cranklike movements around its anterior end as a pivot—in all of these being quite unable to prevent the movement, or, to put it differently, apparently striving all the while for a state of equilibrium which it is unable to find.

The motor disturbances appearing after *unilateral extirpation* of the cerebellum at their period of greatest intensity are: agitation, restlessness, ofttimes whining or groaning, curvature of the spine with concavity toward the operated side, accompanied by tonic extension of the anterior extremity of the same side and spasmodic movements of the three other extremities; spiral rotation of the head and neck toward the sound side accompanied by strabismus and nystagmus of one side, and often by deviation of the eye on the operated side inward and downward, of the other eye outward and upward; a tendency to roll over about the long axis of the body in the direction of the twisting and of the strabismus—i. e., as seen from the back of the animal, from the sound toward the injured side.

Whether these phenomena are caused by the excessive irritation on the cut side, or by the predominance of the sound side over the injured one, The gray matter on each side of the cord is divided into an anterior and a posterior horn. In the lower cervical and in the upper thoracic regions of the cord, as well as in the lumbar region, the lateral portion of the anterior horn becomes partly separated off as a lateral horn (*o*).

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These *cells of the spinal ganglia*, for the most part, are unipolar—i. e., they have but one process which, however, after a short course, splits into two branches. One of the two proceeds toward the periphery and joins the anterior nerve root in a mixed nerve trunk; the other enters the cord by the posterior nerve root. Practically all of the fibers which enter the cord divide into an ascending and a descending branch, both of which give off collaterals, and sooner or later end like the collaterals about the cells of the gray matter of the cord. The peripheral nerve fibers, therefore, have their origin either in the cells of the anterior horn or in the cells of the spinal ganglia.

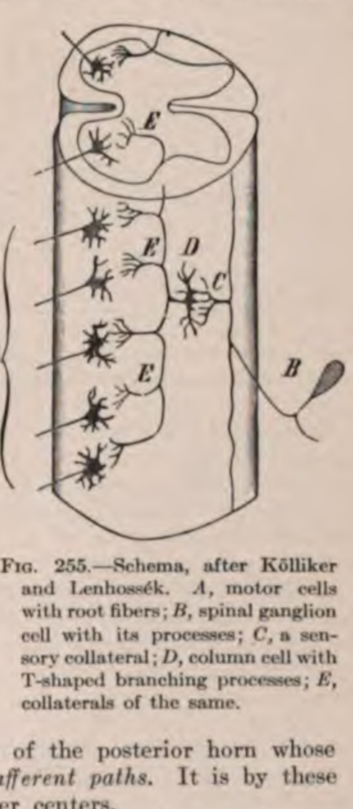

FIG. 255.—Schema, after Kölliker and Lenhossék. *A*, motor cells with root fibers; *B*, spinal ganglion cell with its processes; *C*, a sensory collateral; *D*, column cell with T-shaped branching processes; *E*, collaterals of the same.

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Besides, it is very probable that the optic-nerve fibers entering the anterior corpora quadrigemina play a considerable part in the *reflex excitation* of the nuclei of the eye muscles located along the floor of the aqueduct of Sylvius. The fact that in the monkey, at least, these fibers end in large numbers under and about the aqueduct, and the results of electrical stimulation both favor this view. By stimulating the anterior body of the dog, Adamuk obtained the following movements of the eyes: stimulating on the right side of one body, movement of both eyes to the left; stimulating in the midline, parallel movement of both eyes directly upward; stimulating the posterior side, simultaneous movements downward and inward. Movements of the iris were also observed. After a sagittal section in the median plane, only the eye on the same side was moved. Ferrier has made observations similar to these on the monkey.

Some clinical observations indicate that the posterior corpora quadrigemina are concerned in the propagation of *auditory impressions*, the hearing in the opposite ear being affected in cases where this part is diseased. Bechterew and Flechsig assert, in agreement with this view, that the ganglion of the posterior body receives fibers by way of the lateral fillet, from the cochlear nerve, and v. Monakow has shown that the internal geniculate body is abundantly connected with the posterior quadrigeminal body and sends fibers to the cortex of the temporal lobe. The statements that stimulation of the posterior body in dogs and monkeys evokes a cry from the animal, and that production of voice is stopped by section of that body, lend some weight also.

B. THE CRURA CEREBRI

The crura cerebri, or more correctly the gray matter which forms the wall of the aqueduct of Sylvius, is of special interest mainly because the nuclei of the oculo motor and trochlear nerves are found there.

Fig. 272 represents in a frontal section the *nuclei of the oculo motor* as made out by Bernheimer. It is evident that this nucleus consists of several parts, namely, a lateral chief nucleus, a median nucleus with small cells (*Ke M*) and an unpaired median nucleus with large cells (*Gr Mk*). It is evident from the figure also that the nerve roots connected with the nucleus are in part crossed.

By successive and complete removal of the extrinsic and intrinsic eye muscles innervated by the oculo motor, and by a study of the resulting changes in the nucleus, Bernheimer has reached the following conclusions with regard to the function of its different parts (Fig. 273): The extrinsic muscles are innervated by the lateral chief nucleus, but its cells are not grouped into sharply divided individual nuclei. The small-celled median nuclei (*Ke M*, Fig. 272) supply the intrinsic muscles of the homolateral eye, and the large-celled median nucleus (*Gr Mk*, Fig. 272) belongs to the intrinsic muscles of both eyes.

v. Monakow has made some clinical observations as to the relations of these parts in man, but at present the only conclusions that can be drawn are that the intrinsic muscles (ciliary muscle and the muscles of the iris) are represented in the extreme anterior end of the nucleus, and the extrinsic muscles in the remaining divisions.

Before this Hensen and Völckers had observed, in substantial agreement with the findings of v. Monakow, that stimulation at the posterior end of the floor of the third ventricle gave *movements of accommodation*, and at a

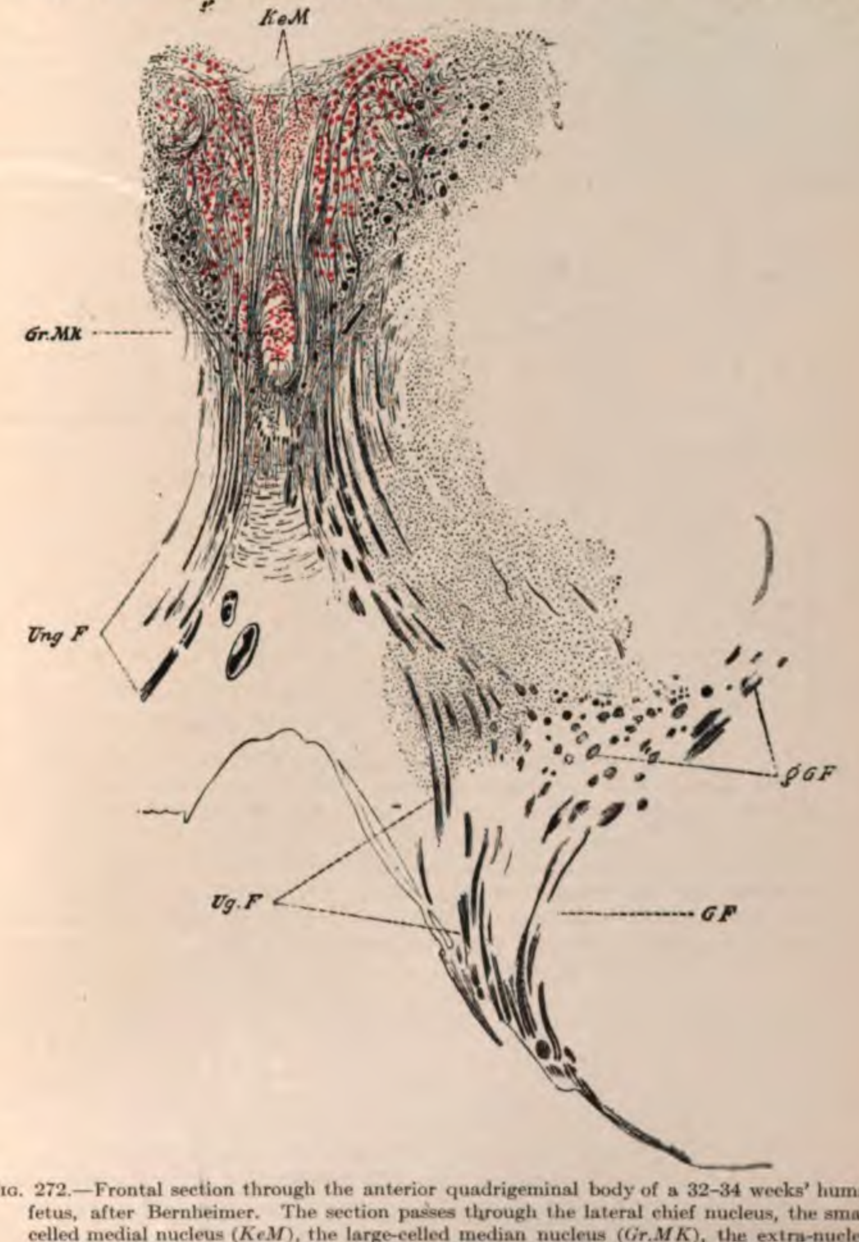

FIG. 272.—Frontal section through the anterior quadrigeminal body of a 32–34 weeks' human fetus, after Bernheimer. The section passes through the lateral chief nucleus, the small-celled medial nucleus (*KeM*), the large-celled median nucleus (*Gr.MK*), the extra-nuclear course of the medial and lateral fibers (*Ung F*, and *Ug. F*) of the third nerve, and the last bit of the extra-nuclear course of the crossed lateral fibers (*GF*). *QGF*, transverse sections of crossed fibers arising from behind and above.

point somewhat farther back gave contraction of the pupil (cf. Fig. 230). Stimulation at the anterior border of the aqueduct of Sylvius gave contraction of the internal rectus, and stimulation somewhat farther back gave in serial order contraction of the superior rectus, levator palpebræ superioris, inferior rectus, and finally of the inferior oblique. When the stimulus was applied to the lateral surface or the deeper parts of the corpora quadrigemina, or to the cut surface of the transverse section in the optic thalamus, the pupil became dilated.

Bernheimer employed a similar method on monkeys. The two halves of the oculo motor nucleus were separated by a median sagittal section and weak electrical stimuli were applied at different points. The results were isolated movements of the different eye muscles innervated from the side stimulated and contraction of the pupil on the side stimulated. The latter effect was obtained only when the stimulus was applied somewhat internal to the median cut surface below the aqueduct and in the anterior third of the region occupied by the anterior quadrigeminal body—i. e., in the region of the small-celled median nucleus (*Ke M*, Fig. 272).

Special observations as to the connections of the two sides of the oculo motor nucleus afford some grounds for believing that the nuclei of the two sphincters (pupil and accommodation) as well as the nuclei of those extrinsic muscles which take part in synergic movements of the eyes, are united. The latter is shown by the fact that synergic movements cease when the paired nuclear region is split in two by a median sagittal section.

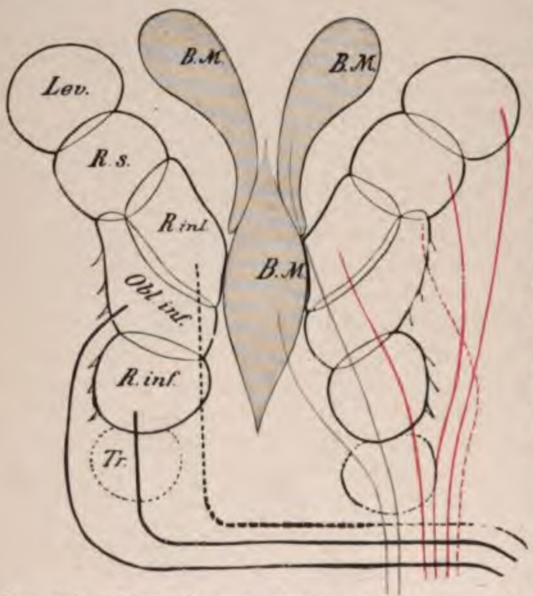

FIG. 273.—Schematic representation of the nucleus of oculo motor nerves, after Bernheimer. The red lines indicate the direct, and the black the crossed root fibers. *B.M.*, intrinsic muscles of the eye; *Lev.*, levator palpebræ sup.; *R.s.*, superior rectus; *R.int.*, internal rectus; *Obl.inf.*, inferior obliquus; *R.inf.*, inferior rectus; *Tr.*, superior oblique.

Complete division of the brain at the anterior end of the midbrain produces a remarkable state of inertness in the muscles, which is described by Sherrington under the name of *acerebral rigidity*. It is recognized by the fact that certain muscles become stiff; the elbows and knees, for example, are rigidly extended, the tail is inflexible, etc. This condition appears to be due to the influence of the afferent nerves from the regions affected, for the stiffness in the arm muscles, for example, entirely disappears after section of the posterior roots for the arm.

Reflex stimulation of an animal in this condition produces certain coördinated movements which are unmistakably related to the movements of locomotion. For example, the left anterior and the right posterior extremities become flexed, while the right anterior and the left posterior are extended at the same time, and vice versa. Not infrequently these reflexes alternate, beginning regularly with flexion of the extremity directly stimulated. At the same time the head and neck are twisted toward the stimulated side; the mouth is opened, the lips and the tongue are retracted, the eyelids opened, the pupil is dilated; the animal utters cries or groans, etc. These reactions, which when the cerebrum is intact usually accompany painful sensations, sometimes appear singly, sometimes in certain combinations.

Rigidity of the triceps muscle can be intermitted by stimulation of the white matter between the anterior and the lateral columns or by stimulation of certain peripheral nerves of the posterior extremity. The effect is felt chiefly on the homolateral side, but to a less extent on the heterolateral side also.

§ 5. THE DIENCEPHALON OR 'TWEENBRAIN

The many connections of the 'tweenbrain with the gray matter of the cerebrum on the one hand and with the afferent nerve tracts on the other speak in most eloquent terms for the great physiological importance of this division of the brain. In fact, all the tracts in which we should expect to find prolongations of the posterior root fibers (the main part of the fillet layer, the superior peduncle of the cerebellum, the longitudinal bundle of the formatio reticularis), and the fibers of the optic tract—all enter the 'tweenbrain, from which in turn they are continued to the cerebral cortex. The latter also sends out fibers to the 'tweenbrain, from which further efferent tracts are given off (Flechsig).

It is possible that the external geniculate body is the point of origin of the efferent optic fibers, and that the reflexes discharged by optic stimuli are here carried over to them.

The experimental and clinical observations on the 'tweenbrain are not of such a kind as to give us even a crude notion of its actual physiological purpose in the normal brain. We can only say that it appears from clinical observations and from the anatomical facts that the different nuclei in this portion of the brain have different functions, and that as a result we have here a fairly sharp localization of different paths and their connections. Hence when the optic thalamus contains a sharply circumscribed lesion, certain afferent impulses are wanting, and for this reason, as v. Monakow observes, many complicated movements are deficient; many others are abnormally performed, certain components being overstimulated, certain others inhibited.

On the other hand the conditions appear to be very favorable for *substitution of functions* in the optic thalamus, so that when lesions are not too extensive the effects are only temporary or may be entirely wanting. This is probably to be explained in part by a bilateral influence of the thalami in which the commissura mollis connecting them together assumes a certain significance.

§ 6. FUNCTIONS OF THE BRAIN-STEM AS A WHOLE

While it is not possible as yet to name the exact functions of the separate centers in the corpora quadrigemina, the optic thalami and certain other parts of the brain-stem, we have some observations on *decerebrated* animals which should afford us some light as to the functions of the hindbrain, 'tweenbrain and midbrain taken together. What the central nervous system is capable of without the cerebrum, considered in connection with the functions remaining after removal of all the parts anterior to the medulla, should give us a general idea of the total powers of the brain-stem.

The lowest vertebrate, *Amphioxus*, has no true encephalon: its brain consists only of a slight enlargement at the anterior end of the spinal cord. Anteriorly and laterally this enlargement embraces a ventricle which is continuous posteriorly with the central canal of the spinal cord. This "brain" contains internally a ganglionic mass and externally a mass of nerve fibers. The former consists mainly of multipolar cells, whose fibers pass over into the fibers of the outer layer running longitudinally of the animal.

Steiner divided this "fish" into two pieces, a head and a tail piece. After some minutes both parts responded to mechanical stimulation by making perfectly regular locomotor movements, at the same time preserving equilibrium and swimming with the anterior end of the piece forward. They fell over on their broad side however as soon as the movement ceased. The animals could even be cut into three or four pieces, and under the circumstances named each part could still make locomotor movements. Steiner's conclusion is that the body of *Amphioxus* consists of perfectly equivalent metameres and has in general no motor center.

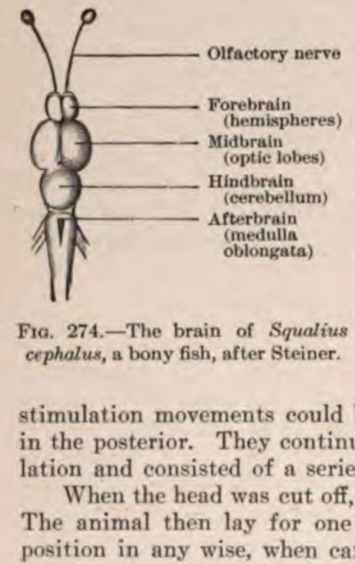

FIG. 274.—The brain of *Squalius cephalus*, a bony fish, after Steiner.

Danilewsky obtained results of very different purport. After division of the animal into an anterior and a posterior half, he noticed in the piece containing the brain occasional "voluntary" movements apparently independent of any external stimulus; while the posterior half remained perfectly motionless. By artificial stimulation movements could be obtained in the anterior half more easily than in the posterior. They continued for from fifteen to thirty seconds after stimulation and consisted of a series of bending and stretching movements.

When the head was cut off, the above-mentioned voluntary movements ceased. The animal then lay for one to two days without spontaneously changing its position in any wise, when care was taken to remove all external stimuli. The reflex movements to artificial stimuli were perfectly normal, but were not abundant, and the irritability of the headless animal was considerably less than that of the isolated anterior half.

Danilewsky concludes from these and other observations that the so-called brain of the *Amphioxus* contains the centers for voluntary motions; destruction or separation of these from the rest of the cerebral nervous system results in loss of motility, providing no external stimulus of sufficient strength acts upon the animal.

In the *true fishes* the cerebrum is but slightly developed, and in the lampreys and bony fishes the cortex consists of only a simple layer of epithelial cells.

After extirpation of the cerebrum from a bony fish (*Squalius cephalus*, Fig. 274) the animal moves exactly like a normal animal, and, according to Steiner, it is quite impossible to discover anything anomalous in its movements. When an earthworm is thrown to the fish, it makes a rush for the booty, seizes it while it is still falling and devours it. A cord of about the same dimensions thrown into the water may or may not be seized, but is never eaten. A decerebrated fish may be even fastidious about its food; spurning fish worms but taking crumbs of bread from the surface of the water. When one red wafer and four white ones are thrown to it, the fish regularly chooses first the red and then the white ones. It does not move to take the food from the observer's hand, but will take it from a long string. Finally, the decerebrated fish will exchange caresses with its uninjured companions. From these observations we may conclude that suppression of the cerebrum in this genus is of no particular consequence—that to judge from the behavior of the animal after the operation, the parts remaining are sufficient for the discharge of all the central functions.

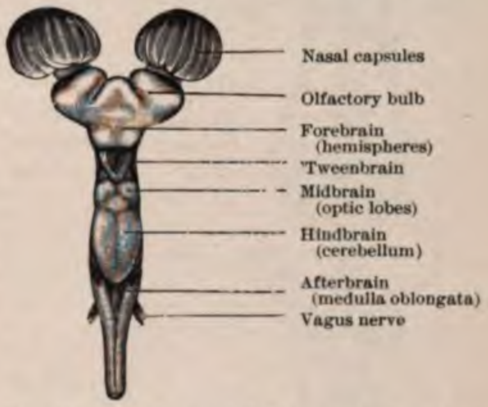

FIG. 275.—The brain of *Scyllium canicula*, a dog-shark, after Steiner.

We have no experiments which give us any clew as to the importance of the 'tweenbrain in the bony fish. But Steiner has reported some in which he removed both the midbrain and the 'tweenbrain along with the cerebrum. Following this operation the animal would lie entirely motionless on its side or on its back, with the fins hanging perfectly limp. Hence we can say that the higher functions of the central nervous system are dependent upon the 'tweenbrain and the midbrain, but just what share each one takes we do not yet know.

The *selanchians* also (dog shark, *Scyllium canicula*, Fig. 275) withstand removal of the cerebrum without suppression of their movements. After a few rounds about the tank the animal lies quietly on the bottom of the tank for many hours or even days at a time, Steiner having scarcely ever seen one in motion when it was not excited by some external stimulus. Besides, the animal does not spontaneously take food, but its inability to do so is not the result of loss of the cerebrum itself, but is rather due to the functional loss of its olfactory lobes,[1] which of course is a necessary consequence of the operation. Careful investigation of the normal dogfish confirms this indication that it seeks food entirely by the sense of smell.

Simultaneous removal of both the 'tweenbrain and the cerebrum likewise produces only insignificant effects. Since this operation involves destruction of the optic nerves, such animals are of course blind; and yet they can swim in a perfectly normal manner. One observes, however, that after some time, which appears to be shorter after removal of the forebrain alone, the animal clings to some corner or wall and, at least so far as observed, never leaves its retreat except when disturbed.

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[1] The olfactory lobe consists of the olfactory bulb and the olfactory tract.—ED.

After removal of the forebrain, 'tweenbrain and hindbrain the dogfish never spontaneously makes any movements. Roused artificially, its movements are effective and perfectly regular, and, so long as it does not leave the normal plane with reference to the direction of gravity, it keeps its balance properly. But let it once get out of the normal position in the water, and its equilibrium is easily lost. It may even come to rest lying on its back. When the animal is suddenly and forcibly placed on its back it makes very evident efforts to regain its normal position, but does not always succeed.

Hence in the dogfish also the so-called spontaneous movements and the finer coördination of movements appear to be bound up with the 'tweenbrain and the midbrain. The lower parts of the brain, however, are alone sufficient to carry out fairly well coördinated movements started by artificial means.

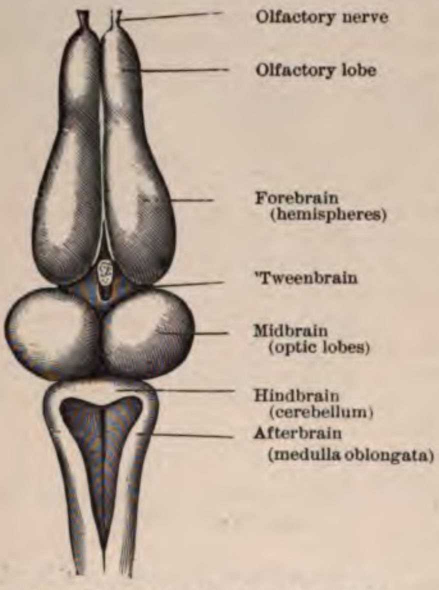

FIG. 276.—The brain of a frog, after Steiner.

Schrader also removed the cerebrum from *frogs* (Fig. 276) without injuring the 'tweenbrain. There was no noticeable effect: the frogs moved about "spontaneously" from one place to another, they swam like perfectly normal animals; at the approach of cold weather they burrowed into the mud or under stones; or, passing the winter in the open, they adapted themselves to external conditions and with the same results as did their normal companions. At the end of the hibernating season, or in summer some months after the wound was perfectly healed, the animals operated upon, just like the normal ones, caught all the flies in the cage, and so on.

But when the 'tweenbrain was injured along with the cerebrum, the same condition appeared as had formerly been described by Goltz as the consequence of removing the cerebrum alone. There were no motor effects strictly speaking, but the animals had lost all their spontaneity. When a frog in this condition was not roused by some external stimulus, it would sit perfectly still, until it dried up to a mummy; it never tried to catch flies, no difference how many were in the cage—it starved to death in the midst of plenty, unless it was artificially fed. Its movements were just like those of a normal frog except that they were perfectly machinelike—a given stimulus always giving the same response. Since the optic nerves were left uninjured by the operation, the animal was influenced by visual impressions, avoiding obstacles by going round them or jumping over them. When it was lowered into and under the water very gradually, by means of a mechanism driven by a screw, the stimulus of the change of medium was not sufficient to cause the frog to move. It simply remained suspended in the water at a depth determined only by the amount of air in the lungs.

We may conclude that in fishes and frogs the central nervous system up to and including the 'tweenbrain is sufficient to regulate all the animal's functions (with the exception, of course, of those directed by the sense of smell) just as in the normal animal. Noticeable changes are produced in the behavior of the dogfish after removal of the 'tweenbrain and the midbrain, in the frog only after injury to the 'tweenbrain.

After taking out the cerebrum of a *lizard* (Fig. 277), Steiner observed no other result than loss of spontaneous ingestion of food and of voluntary movements. When stimulated the animal moved in a perfectly normal manner, avoided obstacles, climbed up the wall of the cage, exhibited no disturbance of the muscular sense, etc. On the other hand it would no longer try to escape when threatened. Likewise, when the cerebrum and the 'tweenbrain both are removed, the lizard can still make perfectly normal movements including leaps of large size. It appears, however, to become quiescent sooner and its movements in climbing seem less accurately regulated than in the animal with the 'tweenbrain intact.

The *turtle* without a cerebrum differs only a little from the normal animal. It makes spontaneous movements, reacts like a normal animal to light rays and is able to estimate visual impressions properly for its own advantage. It is uncertain, however, whether such an animal takes food spontaneously. One such animal, it was observed, left tadpoles placed in its cage untouched for as long as three days. Since, however, an animal whose olfactory nerves only were cut did the same thing, it is possible that here as with the dogfish the determining factor is the sense of smell.

In extirpating the 'tweenbrain from the turtle, it is necessary to destroy the optic nerves; hence the result of the operation is blindness. Nevertheless the animal is able to orient itself in space excellently, and, although it seldom does so, to move spontaneously. Some slight abnormalities also are exhibited in its gait and in the manner of its carriage.

Finally, when the midbrain in addition to the cerebrum and 'tweenbrain are removed, a remarkable phenomenon, first observed by Fano, ensues—namely, an uncontrollable impulse to move about (cf. the similar behavior of the frog, page 604). The animal creeps incessantly in an aimless way; goes back and forth from land to water and from water to land apparently without ever finding a comfortable place. There are, however, unmistakable abnormalities in its move-

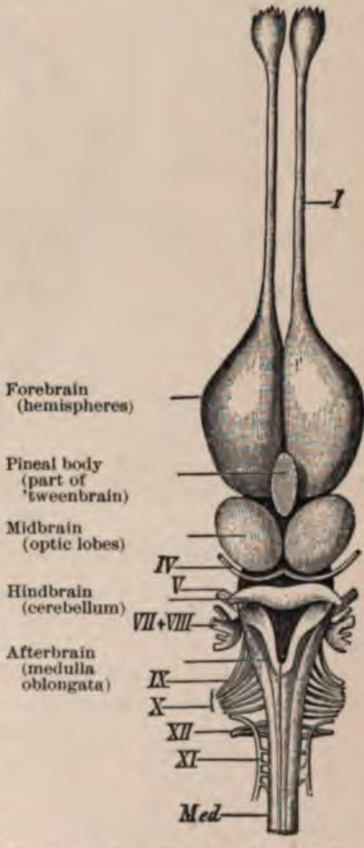

Fig. 277.—The brain of a lizard (*Hatteria punctata*), after Wiedersheim. The cranial nerves are indicated by Roman numerals.

ments: in walking the limbs are lifted too high, extended too far and sometimes are set down too far to one side or the other; the result is that the carapace wabbles from side to side and strikes the floor first with one corner, then with the other.

The chief difference between the *lizard* and the *turtle* and the lower vertebrates after removal of the cerebrum, it would seem, is that they do not spontaneously take food, while the lizard also does not move at all spontaneously. It is likely therefore that the cerebrum is not of the same importance in animals of this grade as it is in the higher vertebrates such as birds and mammals. But even in the latter it can be demonstrated that the lower parts of the central nervous system can maintain a high degree of activity.

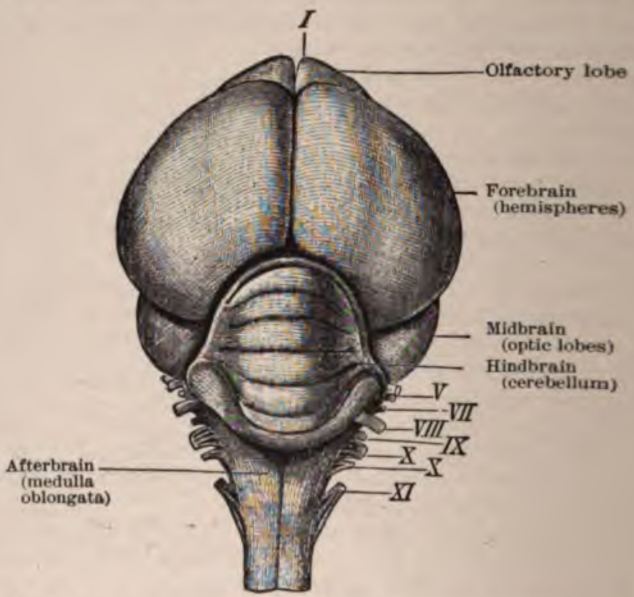

Fig. 278.—Brain of a pigeon, after Wiedersheim. The cranial nerves are numbered.

Of the numerous observations on *birds* which have been made since the time of Rolando, we shall cite only those of Schrader on pigeons. These animals in Schrader's hands survived the operation of removing the cerebrum (Fig. 278) for four to five weeks and died then as the result of progressive general weakness which began about the fourth week.

During the first three or four days they remained in a sleepy condition, standing with feathers ruffled, head drawn in, eyes closed (and often on one leg), just where they were placed. Now and then they would shake themselves, smooth out their feathers with the beak, stretch themselves as if drowsy and, if desiring to defecate, would take a few steps. When thrown up into the air, they made flying movements but came obliquely downward, striking the wall or other obstacles and rather falling to the floor than reaching it by "lighting"; then they once more sank into a stupor. In short, the animals appeared bereft of all initiative, and one would be inclined to declare them blind and deaf and to doubt whether even the sense of touch were intact. But if they came through the first few days, they presented quite a different picture.

They now began to wander about and to keep up a tireless march about the cage. The cadence was a moderately quick step, but frequently as the movement went on it increased in frequency until it became a run, which then tapered off to the usual cadence again, or was sometimes suddenly interrupted and the animal settled down to sleep. It appears that these restless movements were not the result of any abnormal state of excitation, for the same animals which wandered about tirelessly all day spent the night quietly in one spot.

These movements from the first are controlled by sight, for the animal always avoids obstacles about the same as a normal pigeon. They are also regulated by the sense of touch and any temporary disturbance of the equilibrium is regularly compensated by the proper motions.

Only one reaction to auditory impressions was observed, namely that the pigeon drew back at the crack of a match. Various and sundry tones and noises were tried but without any apparent effect.

But the movements of a decerebrated pigeon are readily interrupted by other means: one has only to touch the animal lightly or to lift it and set it down again, and it immediately draws in the head, ruffles up its feathers and falls asleep.

By specially devised experiments it is possible to show that the pigeon is able to coördinate its movements to a definite end. When, for example, one was placed four or five feet from the floor on a small flat surface and a perch was placed one or two yards distant from it, the pigeon flew to the perch and grasped it firmly with its feet. Moreover, when the pigeon was given a choice between flying to the perch and flying to a table some yards farther away, it very decidedly preferred the latter.

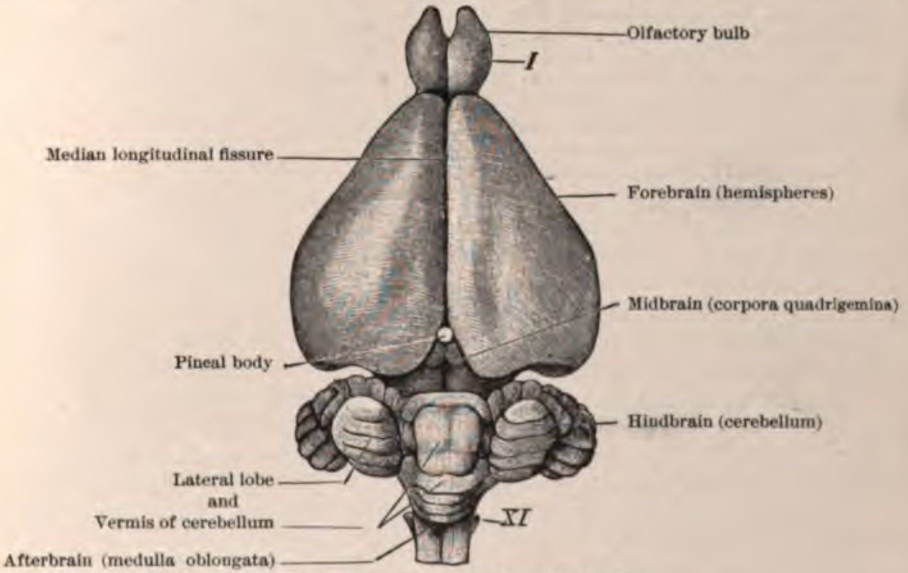

FIG. 279.—Brain of rabbit, after Wiedersheim.

But it never flew up spontaneously from the floor. And it could not be ascertained positively that the decerebrated pigeon ate of its own accord.

Briefly stated, every action of the pigeon without a cerebrum gives the observer a peculiar but perfectly unmistakable impression of an automaton. Its actions are very diverse and very complicated, but under given circumstances can be very definitely predicted with a high degree of certainty. The decerebrated bird moves therefore in a world of objects, the position in space, size, configuration of which determine the character of its movements, but which are otherwise entirely without meaning to the bird. One thing like another is a mere space-filling mass: it avoids or pushes aside another pigeon as it would a stone. A cat or a dog means no more than an inanimate object. A decerebrated male coos like a normal male and exhibits evidence of sexual desire—but his affections are entirely objectless. It appears to be a matter of indifference to him whether a female is present or not. In the same way a female shows no interest in her young. If full-fledged, they follow the mother, screaming incessantly for food; but they might as well address their entreaties to a stone.

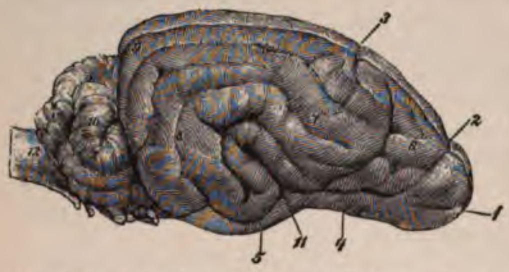

FIG. 280.—Lateral view of the dog's brain, showing the different lobes of the cerebrum, after Ellenberger and Baum. 1, Olfactory lobe; 2, boundary between the olfactory and frontal lobes; 3, boundary between the frontal and parietal lobes (cruciate fissure); 4, olfactory tract; 5, piriform lobe; 6, frontal lobe; 7, parietal lobe; 8, temporal lobe; 9, occipital lobe; 10, cerebellum; 11, boundary between the parietal and temporal lobes (fissure of Sylvius); 12, medulla oblongata.

The functions left, however, are very important ones. To what extent they depend upon the 'tweenbrain cannot, for want of critical attention to this point, be definitely stated. But from Schrader's observation that animals in which the optic thalami were injured extensively in removing the cerebrum stumbled over very slight obstacles and did not correct the positions of their limbs immediately when they were displaced, it seems probable that the 'tweenbrain plays an important rôle in all these functions.

Among *mammals* we have observations on the complete removal of the cerebrum from *rabbits* and *dogs* (Figs. 279 and 280).

According to Christiani, rabbits with the cerebrum removed sat immediately after the operation just as normal animals are careful to sit, and when attempts were made to catch them by the hind leg they ran. Spontaneous movements were also occasionally made. But when they were not disturbed in any way and were protected from powerful stimuli, they easily fell asleep. They woke from this sleep without being roused externally. They walked about for a long time but finally came to rest and went to sleep again. There was nothing abnormal in any of these movements: the animals avoided obstacles without touching them; they made stops in the midst of their wanderings; they climbed and sprang upon objects; etc.

The rabbit therefore can also regulate its movements quite normally without a cerebrum and can use its visual sense for this purpose. We have no more exact observations on their behavior, as the animals in these experiments were not observed for more than twelve hours after the operation.

It appears from Christiani's observations that this regulation is the work of the 'tweenbrain, for in rabbits deprived of this part, or in which it was extensively injured, the coördination necessary for locomotion and for maintaining the equilibrium in sitting and standing was entirely lost.

Much more significant than these observations are those of Goltz on a decerebrated *dog* which survived the operation for a long time. In this dog, whose history we shall now relate, not only was practically all the cerebrum destroyed, but the 'tweenbrain and to a large extent the corpora quadrigemina on the left side as well. The functions carried out by this dog were therefore probably less extensive than would be possible if the cerebrum only were extirpated. Since this experiment is of the utmost importance for a proper conception of the functions of the central nervous system, we shall report it somewhat extensively.

The left hemisphere of this dog was removed in two operations on the 27th of June and the 23d of November, 1889, the entire right hemisphere was removed in one operation on the 17th of June, 1890. The dog lived until December 31, 1891, when he was killed by bleeding, and was therefore under observation for a year and a half after the last operation. Fig. 281 is a picture of the brain as it appeared at autopsy.

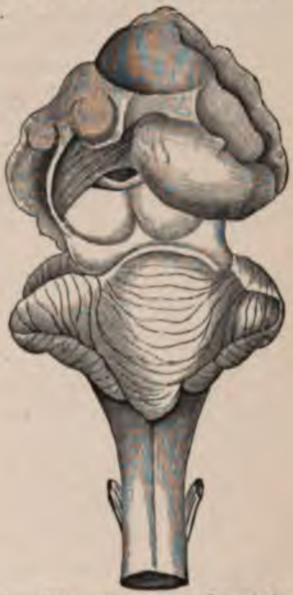

FIG. 281.—The remainder of the brain of Goltz's dog, after removal of the cerebral hemispheres. The medulla, pons, cerebellum and the roots of all the cranial nerves connected with the medulla and pons were perfectly normal. The corpora quadrigemina were somewhat degenerated. All that was left of the cerebral cortex was a small portion of the temporal lobe on each side.

On the third day after the last operation (June 20, 1890) the animal walked about the room without falling. From this time on his strength increased so rapidly that on the 22d of July he easily climbed up an inclined plane of twenty degrees. The ability to perform crude muscular movements was therefore perfect.

After some months considerable *disturbance in nutrition* made its appearance, the hind parts becoming more and more emaciated. By feeding the animal heavily this progressive emaciation was finally overcome, but the certainty of the dog's movements, which was so plain a feature for a few weeks after the operation, did not return. In spite of this until a few days before his death he was able to raise himself on his hind legs and to place his paws on the grating of his cage.

According to Goltz himself the cause of this emaciation lay partly in the fact that the animal continually moved about in his cage and that he never rested nor slept so long as a normal animal. It is probable also that it was due to imperfect heat regulation, since the heat loss was greater than normal. At any rate it is stated that the skin was noticeably warm. Otherwise, judging by nothing more than the fact that the animal lived so long, the heat regulation must have been fairly good. When the dog slept, he curled up as normal dogs do; in a warm room he panted and stretched out his tongue; and in a cold room he shivered.

Digestion went on normally: the tongue and the teeth were normally preserved; there was no foul odor from the mouth; the fæces were of normal color and consistency. No observations were made as to the utilization of foodstuffs. The urine contained no proteid nor sugar. The animal (a male) gave no evidence of sexual heat.

The cruder movements, such as *locomotion*, were fairly normal and the gait on a rough floor was tolerably good. On a smooth floor the animal slipped very easily, but recovered his feet without help. He never walked on the backs of his feet; and immediately straightened them when his toes were forcibly turned under.

Placed on a table with one foot over a trapdoor, the dog allowed the foot to follow the trap for a distance as it fell, but did not lose his equilibrium.

It happened once that the dog had one hind paw injured. Until the paw was completely healed he hopped about on three legs, keeping the injured member voluntarily lifted from the floor.

Hence the bodily movements were regulated in many different ways. And yet his movements were not very precise, for when he was pinched he could not purposely reach the place. If for example he was pinched on the left hind foot, he would snap to the left, but seldom caught the offender's hand.

The *sense of touch* was noticeably dull. When by means of a fine tube air was blown between the hairs on the back of his foot, he did not move; he was likewise insensitive to blasts on his nose. But certain parts of the skin, as for example, the interior of the ear, proved to be extremely sensitive. He responded promptly to stronger cutaneous stimuli and could be awakened from his sleep in this way. If while he was walking about he was pinched anywhere, he gave evidence of his displeasure by various expressions of the voice, or even snapped.

In order to test the *sense of taste*, Goltz made the following experiment. He placed some horse meat in each of two dishes. To the one he added milk, the other he covered with an extremely bitter solution of quinine. He fed the dog several pieces of the meat wet with milk, one after the other, by simply holding them close to his nose. They were seized, chewed and swallowed. Suddenly he offered him a piece from the quinine dish. It also was seized and chewed once; then the dog made a wry face and spat it out.

The *sense of smell* was of course lost. It was only by stimulation of the branches of the trigeminal nerve that pungent odors had any effect on the animal.

Auditory sensations were very much blunted, although it was possible to rouse the animal from sleep by a purely auditory stimulus.

The *sense of sight* was practically lost. The pupils of both eyes contracted when light was thrown into them, and the eyes were closed when a dazzlingly bright light from a bull's-eye lantern was thrown in the dog's face. In rare cases he turned his head to one side. That was all. He was unable with the aid of vision to avoid obstacles placed in his way; and the blank, idiotic expression of his eyes never changed in the least when threatening gestures were made or a strange dog was held so that the images must have been formed on the retina.

The animal's *intelligence* was very much reduced. He was so stupid that on the last day of his life he raised a howl when he was lifted out of the cage to be fed, just as he had done for months. He never gave any expression of joy and only showed displeasure when he was pinched or handled roughly. Once when he had gone without food for a longer time than usual, he made sounds indicating his impatience. He also ate more voraciously than usual. But when he had eaten his fill, he stopped and lay down to rest or to sleep.

He never learned to lick himself dry when he became wet, so that he shivered much from cold at times. He likewise never tried to hold a bone with his fore paws.

In view of this it is the more remarkable that the animal again acquired the ability to eat and to drink. For a long time it was necessary to push the food far back in the animal's throat, for when it was merely laid on the front end of his tongue it was neither chewed nor swallowed. On the twenty-third day after the last operation it became unnecessary to push the food so deep into the mouth. It was seized by the tongue and carried back when placed pretty well forward in the mouth. Gradually the dog got better control of his jaws, and finally had made such progress that he could drink a large bowl of milk when his snout was held close in it, and could eat meat when the dish was placed so that his snout touched the food. The reason for touching the food will be apparent when we remember that the sense of smell was entirely lost and the sense of sight reduced to almost nothing.

The following experiment shows that the animal could do a rather more difficult task. A small blind alley was made by means of two boards placed endwise against the wall. When the dog was let into this alley, which was so narrow that he could not turn round in it, he walked to the end and reached up on the wall, "trying" in vain to get out. Finally he began to walk backward, and after about twenty minutes managed to back all the way out, although the length of the alley was only about twice the length of the animal.

It follows from these observations that a dog without his cerebrum is able to carry out all of the functions necessary to life, if only his food be placed immediately in front of his nose; that he is still able to perform locomotor movements satisfactorily; that these movements are influenced and regulated by the muscular and tactile senses; also that the sense of hearing and the sense of sight, although in a very slight degree, can influence his movements. Finally, his behavior during hunger and after taking food teach us that the bodily desires are still "felt." The cerebrum we must conclude is not necessary for any of these functions, nor for passing from the sleeping to the waking condition and *vice versa*.

Flechsig was able to determine on a *human* monster, in which only the lower parts of the brain up to and including the posterior corpora quadrigemina were developed, that these findings for the dog apply at least in part to man. The child lived for a day and a half and during this time gave various signs of discontent. It whimpered occasionally and its whimperings became more vigorous and various movements of its limbs became more active when its skin was pinched.

The observations here brought together on the effects of removing the cerebrum from different vertebrates may be summarized briefly as follows: *these effects are very slight or even unnoticeable in the lowest vertebrates, but the higher we ascend the scale of animal life, the more pronounced and extensive they become.* But even in the highest of the lower animals studied (dog), the functions of the central nervous system which remain are sufficient to maintain all the vital processes necessary for life, with the single exception of seeking food. The effects are chiefly upon the highest powers of the nervous system, especially upon those which we comprehend as belonging to consciousness. For these powers the cerebrum in the highest vert [illegible] at plays the determining part, and cannot be replaced by the lower nerve centers. With regard to the state of consciousness in decerebrated animals, it is evident that no proposition can be laid down which is entirely free from objection, and there is no occasion here to discuss the hypotheses bearing on the subject which have been put forward.

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CHAPTER XXIV

PHYSIOLOGY OF THE CEREBRUM

It has long been assumed that the brain represents the material substratum of the psychical activities. Descartes regarded the pineal gland as the seat of the mind; Willis located perception in the corpora striata, imagination in the corpus callosum, and memory in the convolutions; and Cabanis expounded his doctrine that the brain secretes thought in the same way as the liver secretes bile.

Gall was the first to get a deeper insight into the significance of the brain as the substratum of the psychical life of man, and he undertook to prove this doctrine by actual observation. As Flourens, the most positive opponent of Gall, put it, this doctrine existed in science before Gall, but after him it ruled there. Investigating each sense by itself, Gall excluded all of them, one after the other, from any direct participation in the powers of intelligence. So far from being developed in proportion to the intelligence, most of the senses he saw are developed exactly in inverse proportion thereto. Taste and smell are sharper in the mammals than in man, sight and hearing are more keenly developed in the birds than in mammals; but the brain is everywhere developed in direct proportion to intelligence. Intelligence remains after loss of sight and of hearing and would probably survive all the senses.

The brain therefore is the only organ of the mind. It consists however of many different parts, and the question naturally arises whether all of these parts are of the same importance for the psychical activities. Gall and his pupils had the idea that only the cerebral hemispheres represent the substratum of the mind, and from what we have learned in the preceding chapter, and as we shall prove more fully in this one, we can now make this affirmation with much greater definiteness. The lower parts of the brain probably have no direct significance for the psychical functions. As has been observed in the preceding chapter, their purpose seems to be rather to regulate quite independently of the consciousness and of the will a number of the purely vegetative functions and to connect the cerebral hemispheres with the remainder of the nervous system.

Gall however was not satisfied merely to have demonstrated the importance of the brain for the psychical life, but proceeded to work out a detailed psychology which he endeavored to bring into line with his ideas concerning the functions of the brain.

Gall's psychology subdivided the intelligence into a number of different faculties entirely independent of one another, each of which had its own power of perception, memory, judgment, imagination, etc.

The most positive objections can be raised against this conception of the mental personality of man as an aggregate of arbitrarily chosen and independent faculties. This was early realized by Flourens who, in direct opposition to Gall, laid great emphasis on the unity of the ego. Moreover, the faculties which Gall postulated were not coördinated with each other, but were of all possible and impossible kinds. Some were partly metaphysical, some related to the emotions and some stood in direct connection with the sensations.

It is practically certain that Gall's psychology would never have attracted any further notice if he had not attempted also to locate the organs for the different faculties in different parts of the brain.

His point of departure was an observation which he had made as a student. He thought he had discovered that those of his fellows who had a good memory for words had prominent eyes. Hence the organ for this faculty must be situated above and behind the eye sockets. He conceived that the organs of the different faculties lay only on the surface of the brain, also that wherever a certain organ was especially well developed the skull at that point was bulged out.

Hence if one were to observe the most characteristic peculiarities in the traits and the character of many different individuals and were to study their skulls, one could determine the exact location of the separate organs. Then nothing would be simpler than to determine a person's character and the quality of his endowments by examining his skull. What a broad and extremely interesting perspective this simple and (in the fullest meaning of the word) palpable doctrine opened up! And how extraordinarily useful *phrenology*, as the new science was called by its disciples, would be in education and in the choice of a life work!

Gall was unquestionably a good observer, and in many points the fundamental principles of his method were not far wrong. But this did not prevent him from losing all critical sense and discretion when it came to determining empirically the location of his "organs." Gall's own writings and those of his followers furnish the most flagrant examples of this; nevertheless his doctrines were for a long time espoused in certain quarters with the greatest confidence.

In science phrenology soon had its day, and since Flourens published his researches on the functions of the brain (1822), it has belonged among the curiosities of the scientific lumber room.

Flourens' works declared that only the cerebral hemispheres were of any direct importance for intelligence. He laid down the following propositions, which are given here in his own words: (1) One can cut away from the front, the back, the top and from the sides, a fairly large part of the cerebral hemispheres without destroying the intelligence. Hence a rather limited portion of the brain is sufficient for the exercise of its mental functions. (2) The more one removes of the brain substance the more is the intelligence weakened, and its powers proportionally restricted. When a certain limit is passed the intelligence vanishes altogether. For the complete development of the mental powers therefore all the different parts of the cerebrum work together. (3) When one particular function is lost, all are lost; when one faculty vanishes, all vanish. There are no different organs for the different faculties or sensations. The ability to perceive, judge, or will one thing has its seat in the same point as the ability to perceive, judge, or will another. This ability, which in its essence is one and indivisible, has its seat in a single organ.

For more than a decade the conception expressed in the propositions above, partly owing to the reaction against phrenology, partly owing to the weight of Flourens' investigations on the physiology of the nervous system, was regarded as the last word of science with regard to the relation of the mind to the brain. This is not, however, the modern conception.

There was indeed a modicum of truth in phrenology. Not that its positing the different intellectual qualities in definite regions of the brain was correct, nor that its postulate that the form of the skull, its curvatures and prominences, gives expression to the functional capabilities of the underlying parts, has been found to accord with fact. In this respect phrenology has been relegated far to the rear, we hope for once and all. But further research has demonstrated that the cerebral hemispheres have not one and the same function in all of their parts; it has shown that in the production and elaboration of the different kinds of sensations as well as in the influence of the cerebrum on the functions of the body, entirely different areas of the hemispheres are active.

We may go farther and say that we have certain grounds for believing that different sections of the cerebrum participate in the different mental processes; yet the modern doctrine of *cerebral localization* is at bottom something quite different from the old phrenology. Phrenology assumed that there were a number of different organs in the brain, each specifically set aside for some complex function, although that function was sometimes purely metaphysical. The new doctrine has been content to establish first of all the importance of the different parts of the brain for the functions of the body and for the sensations produced by stimulation of the afferent nerves. It has, it is true, ventured a step farther and has sought to bring the activity of the mind under physiological investigation. But these investigations aim to discover how the psychical functions can be carried out by the coöperation of the various parts of the brain—exactly the reverse process, therefore, of the phrenology of Gall. Finally, the spirit of modern research is poles asunder from the spirit of phrenology: it will not forcibly warp the facts into line with preconceived ideas and arbitrary hypotheses; but it seeks to be entirely free from bias, and in this spirit to determine by observation and experiment the facts which may be able to help us on toward a deeper theoretical comprehension of the cerebral functions.

As early as 1825, Bouillaud tried to show that lesions of the cerebral hemispheres involved loss of the coördinated movements necessary for speech only when the most anterior divisions of the brain, the frontal lobes, were affected. Somewhat later (1836) Marc Dax stated that articulate speech was controlled by a place in the left half of the brain. But his ideas received no encouragement—in fact they were described as pseudo-scientific. In 1861, however, Broca made definite observations on some diseased cases and was able to establish the fact that (in right-handed persons) destruction of the third frontal convolution of the left hemisphere abolishes the power of speech.

These statements were soon corroborated by observations on similar cases by other authors, and thus, contrary to Flourens' doctrine, a functional differentiation of the cortex into different regions was demonstrated. But there was considerable hesitation about giving up the doctrine of the unity of the brain, and it was not until investigations had been carried much further that it was finally overthrown.

On purely anatomical grounds Meynert concluded that the anterior part of the cerebral hemispheres was more closely related to motion and the posterior part to sensation. Then came (1870) the work of Fritsch and Hitzig by which it was established for all time that different parts of the hemispheres actually have different functions.

Among the many articles of faith which had long been held with regard to the brain, was the belief that the cerebral cortex was nonexcitable electrically—i. e., that no visible effect could be produced by application of the electric current to the cortex. Fritsch and Hitzig showed that this idea was wholly erroneous and demonstrated that by electrical stimulation of the cortex muscular movements could be obtained; but that they could only be obtained when the current was applied to certain definite portions. The resulting movements appeared in various groups of muscles—those of the face, the fore or the hind leg, etc.—according to the exact point, within the general area, which was stimulated. From other portions of the cortex the current produced no visible effect.

These discoveries excited the greatest interest and led to many new researches of various kinds which both served to establish the doctrine of different physiological functions for different cortical regions, and at the same time to greatly broaden and deepen our knowledge of the cerebral functions.

Since very little is known with regard to the physiological purposes of the basal ganglion (e. g., the nucleus candatus, nucleus lentiformis, the gray masses of the claustrum, etc.) belonging properly to the cerebrum, we shall pass over them here and in this chapter shall consider first the motor and sensory areas of the cortex, and then take up the psycho-physical functions of the cerebrum.

FIRST SECTION

THE MOTOR AND SENSORY AREAS OF THE CORTEX

§ 1. THE MOTOR AREAS

A. GENERAL SURVEY

The results of Fritsch and Hitzig to which we have referred on the preceding page were as follows: No movements were obtained by stimulation of the posterior part of the cerebral cortex with weak electric currents. But when the current was applied to the anterior part, movements appeared on the opposite side of the body. With a weak stimulus the effect was confined to certain sharply defined groups of muscles. With a stronger stimulus the movements appeared also in other groups on the same side (cf. Fig. 282).

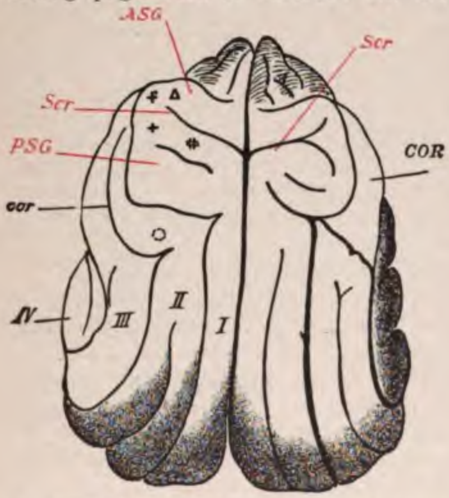

Fig. 282.—Dorsal surface of the dog's brain, with the excitation points indicated according to Fritsch and Hitzig. Δ, neck muscles; +, extensors and adductors of the foreleg; +, flexion and rotation of the foreleg; ♯, hindleg; ○, face; *Scr*, sulcus cruciatus; *ASG*, anterior sigmoid gyrus; *PSG*, posterior sigmoid gyrus; *COR*, coronary gyrus; *cor*, coronary fissure; *I*, *II*, *III*, *IV*, first to fourth external convolutions.

With rapidly repeated induction shocks applied to the different points, the appropriate muscles could be thrown into tetanus. Continued for several seconds, this form of stimulus produced a persistent tetanus which might spread to all parts of the body (cortical epilepsy, cf. below, page 641).

The first question suggested by these observations is, what part of the cerebrum is the part primarily stimulated by the current—the cortex, the underlying white matter, or the deeper parts of the brain?

The answer is unanimous, that the cortex represents the immediate point of attack. The following are among the most important experimental proofs of this proposition:

In the first place it may be observed, that if the current took effect on the lower parts of the cerebrum, muscular movements should be obtained by application of the current to widely different regions of the cortex. Since this is not the case, it is merely a question between the cortex and the subjacent white matter. The following facts speak against the latter possibility:

(1) Under certain circumstances it is possible to stimulate the cortex mechanically, but the white matter cannot be so stimulated (Luciani and Tamburini). (2) It requires a stronger current to stimulate the corona radiata electrically than to stimulate the cortex. (3) On the other hand a muscular contraction caused by continuous stimulation of the cortex ceases decidedly sooner than after stimulation of the corona (Levy). (4) After poisoning with chloral (Franck and Pitres), the cortex becomes inexcitable, but movements can still be obtained from the corona. Likewise the cortex is rendered inexcitable to a depth of 2–3 mm. by painting it with cocain (Carvalho).

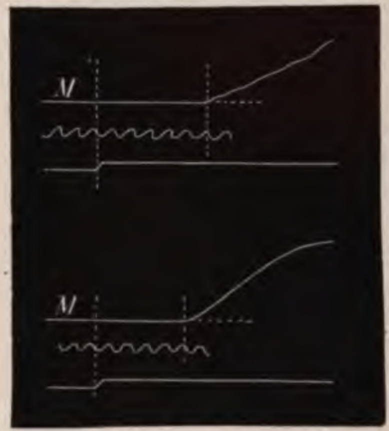

FIG. 283.—Latent period of muscular contraction induced by stimulation of the cortex (upper tracing), and by stimulation of the underlying white substance (lower tracing), after Franck. The time record in each case is in 1–100ths of a second. The instant of stimulation is indicated by the vertical line to the left, the beginning of the contraction by the vertical line to the right.

Again when a certain muscular contraction is aroused first from the cortex and then from the corona and the first two responses are recorded, it is found that the latent period of the first is considerably longer than that of the second —e. g., cortex, 0.065 second; corona, 0.045 second (Franck). The difference of 0.02 second is doubtless due to a delay in the excitation process occasioned by the nerve cells (Fig. 283). The facts also that the contraction curve following cortical stimulation rises more slowly and is not so regular as that following stimulation of the corona, and that cortical stimulation is accompanied by a clonic[1] contraction, while stimulation of the corona is not, are probably to be explained by the presence of nerve cells.

Hence it is conceivable that the electrical stimulus acts directly on the large pyramidal cells of the cortex (cf. Fig. 284, right side Nos. 4, 5, 6) although this would not mean that there might not be other points of attack, as, e. g., the end arborizations of the afferent nerves as well.

These things being so, we may say that certain definite regions of the cortex stand in a more definite relation to the movements of the body than do other parts of the brain. These regions are described as the *motor cortical areas* of the cerebrum.

B. STIMULATION OF THE MOTOR CORTICAL AREAS IN DIFFERENT MAMMALS

It would lead us too far afield to describe here in detail all the results obtained by electrical stimulation of the cortex in the different mammals.

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[1] By clonic contraction is meant one whose strength is conti

of various kinds which both served to establish the doctrine of different physiological functions for different cortical regions, and at the same time to greatly broaden and deepen our knowledge of the cerebral functions.

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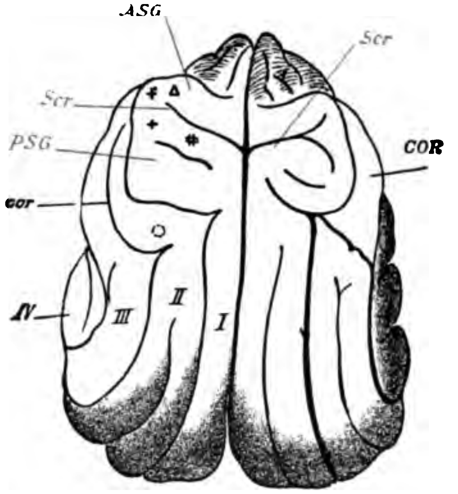

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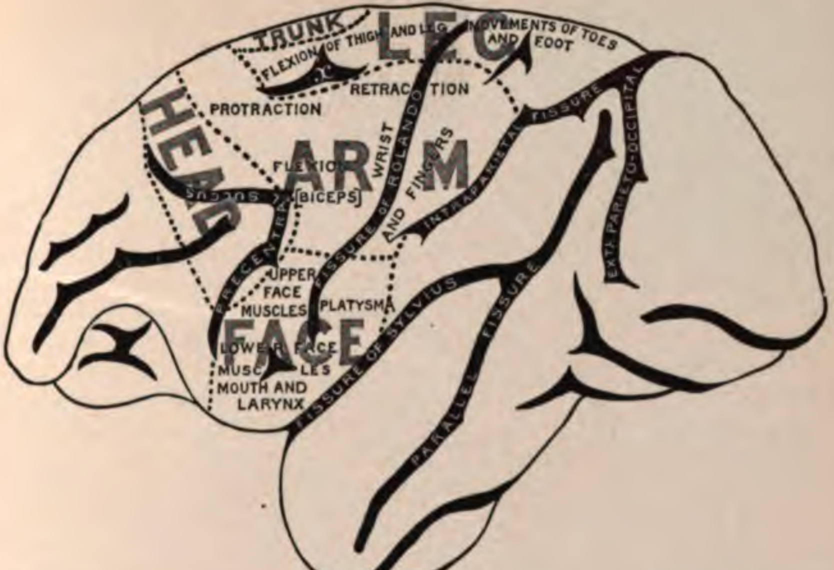

FIG. 285.—Motor cerebral localization in the monkey (*Macacus sinicus*), after Horsley and Schäfer. Outer surface of left hemisphere.

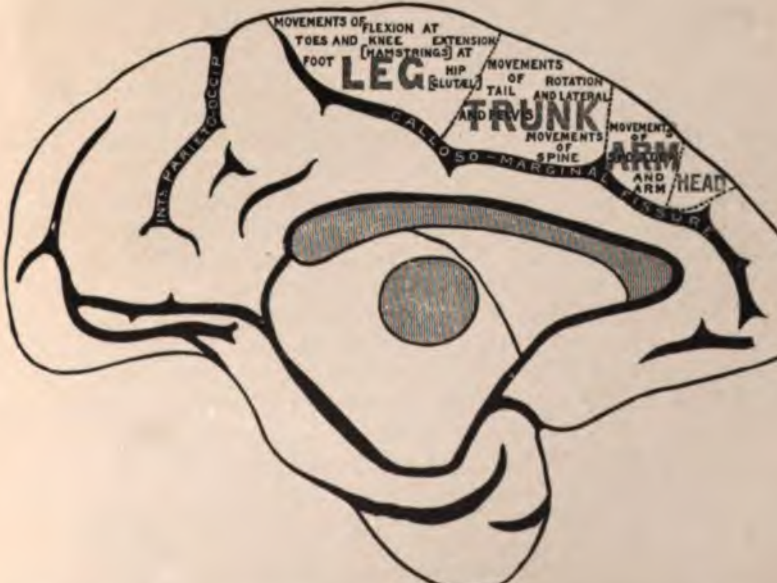

FIG. 286.—Motor cerebral localization in the monkey (*Macacus sinicus*), after Horsley and Schäfer. Inner surface of the left hemisphere.

thus the lower part of the two central convolutions is related to the musculature of the face, the middle part to that of the anterior extremity, and the upper part to the muscles of the posterior extremity. On the very edge of the hemisphere is an area for the movements of the trunk. That portion of the motor zone lying immediately in front of the anterior central convolution is adapted for movements of the head and eyes.[1]

In the gyrus marginalis on the medial surface of the hemisphere we find in serial order from anterior to posterior areas for the *head*, the *anterior extremity*, the *trunk*[2] and the *posterior extremity*.

On closer investigation of the subject we find that within each of the cortical areas for the greater divisions of the musculature, a specialization like that shown diagrammatically in Fig. 287[3] can be demonstrated.

The movements obtained by cortical stimulation are in many respects similar to voluntary movements. As a rule they represent the combined action of several groups of muscles; they are seldom performed by a single group and never by a single muscle.

In stimulating the cerebral cortex of the monkey Sherrington observed that simultaneously with the contraction of certain eye muscles, the tonus of the *antagonistic muscles* decreased (cf. page 640). This is by no means an isolated phenomenon, for according to further observations by Hering, Jr., and Sherrington, it appears to be a general rule that on stimulation of a definite point in the cortex, contraction of the appropriate muscle is accompanied by relaxation of its antagonist. For example, on stimulation of the point in the cortex for extension of the elbow, one gets contraction of the *triceps* group and at the same time relaxation of the *biceps*, or on stimulation of the point for extension of the fingers, one gets contraction of the *extensores* and relaxation of the *flexores digitorum*, etc. These authors declare that in the monkey they never observed simultaneous contraction of true antagonists, such as the extensor and flexor of the elbow. The simultaneous contractions of antagonistic muscles described by other authors might have been due among other things to diffusion of the stimulus from one cortical field to another lying near it.

When a stimulus applied to a given field in the cortex produces movements in other muscles than those corresponding strictly to that field, it is observed that the *movement always spreads* first to other muscles of the same member—e. g., contractions of the shoulder muscle are accompanied by movements in all the muscles of the anterior extremity even down to the fingers. If the initial contraction be in the muscles of the thumb, the movements spread farther and farther up the arm to the wrist, elbow and shoulder.

The contributions of Beevor and Horsley on the motor zone of the *orang-*

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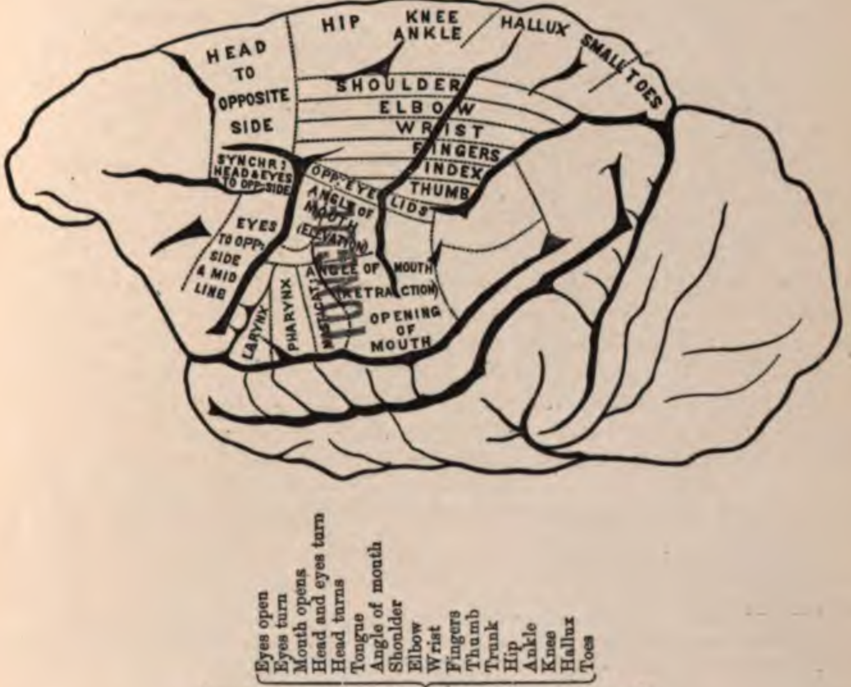
[1] According to Bechterew, contractions of the brow, closure of the lids, and movements of the ear are also obtained from this part of the cortex.

[2] According to H. Munk, the cortical area for the musculature of the trunk lies in the frontal lobe.

[3] For the sake of simplicity, the different fields in this figure have been represented as if they were sharply distinct from one another, whereas in reality there are no sharp boundaries demonstrable, either between the smaller areas or the larger areas. One field always passes gradually into the other.

outang, and those of Sherrington and Greenbaum on the *orang-outang*, *gorilla* and the *chimpanzee*, are of very great interest partly because these anthropoid apes stand closest in the scale to man himself, and partly for the special reason that a further progressive development of this zone from the monkeys to the highest apes is therein unmistakably demonstrated. The fact of this development teaches us in the clearest possible manner how careful we must be in applying the results obtained from other animals to man himself.

The general division of the motor zone as it has been made out in the monkeys is the same in its larger features for the apes. There are however several very noteworthy differences between the two groups. In the monkeys (cf. Fig. 285) we find on the convex surfaces, both on the central and the frontal convolutions, single excitable regions from which several kinds of movements can be discharged. In the apes (cf. Fig. 288) the region on the frontal convolutions contains but one field from which only movements of the eyes can be induced. The posterior central convolution is entirely or in very large part inexcitable, the motor cortical areas being for the most part gathered together in the anterior central convolution. Again, whereas in the monkeys there are *no sharp demarcations* between the cortical areas for *different groups* of muscles, in the orang-outang the cortical areas for the main divisions of the body are separated by regions which are inexcitable.



Arrangement of excitable fibers in the internal capsule.

Fig. 287.—Motor cortical areas in the monkey (*Macacus sinicus*), after Beevor and Horsley.

While the isolation of smaller areas within any larger area, as of the arm or the leg, is not so marked as this localization of group areas, it is nevertheless much sharper than it is in the monkeys; for when contraction is induced by stimulation of a definite point, it is as a rule confined to one definite group of muscles and does not spread as in the monkeys to all or most of the muscles of the same member.

For purposes of diagnosis the *exposed cerebral cortex of man* (Figs. 289 and 290) has in rare cases been stimulated electrically, and results have been obtained which in general agree with observations based on cortical lesions, as well as with the above-described results on the manlike apes. The motor cortical zone of man probably consists therefore of the *anterior central convolution*, the posterior part of the *frontal convolutions* and the *paracentral lobule*. Within this zone the areas for lateral movements of the head and eyes are located in the posterior part of the second frontal convolution; the face musculature is represented in the lower part of the anterior central convolution, the muscles of the upper extremity in the middle part, and those of the lower extremity in the upper part. The paracentral lobule in each hemisphere (Fig. 290) seems to be associated with both opposite extremities. Above the cortical area for the upper extremity is found the area for the musculature of the trunk.

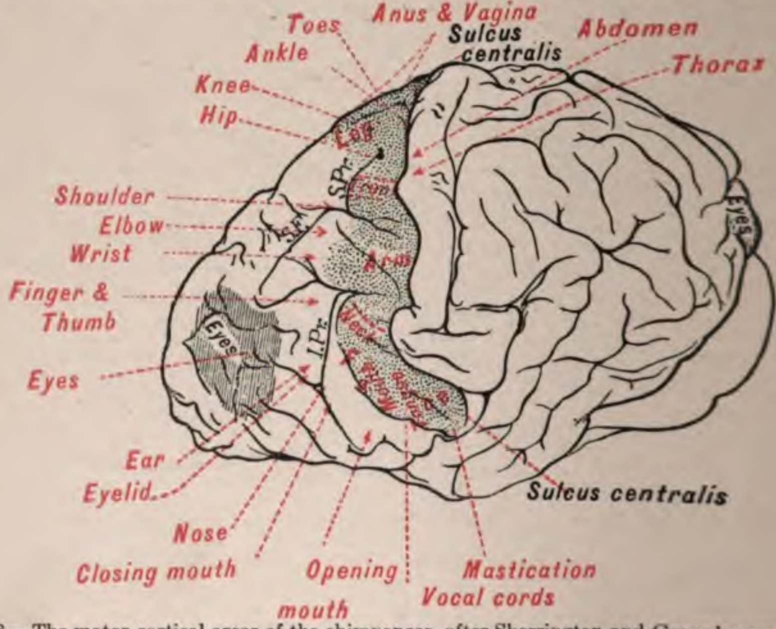


FIG. 288.—The motor cortical areas of the chimpanzee, after Sherrington and Greenbaum. The extent of the motor zone is indicated in black. The red arrows indicate the region in which the special areas are to be found.

It is probably not too much to suppose that the smaller areas within each of these larger areas have the same general arrangement as have those of the apes.

Moreover, it is found in these stimulation experiments on man that, just as in the manlike apes, the *localization is very sharp,* that the movements indeed are confined to single groups of muscles, and that between the excitable points are regions which are inexcitable.

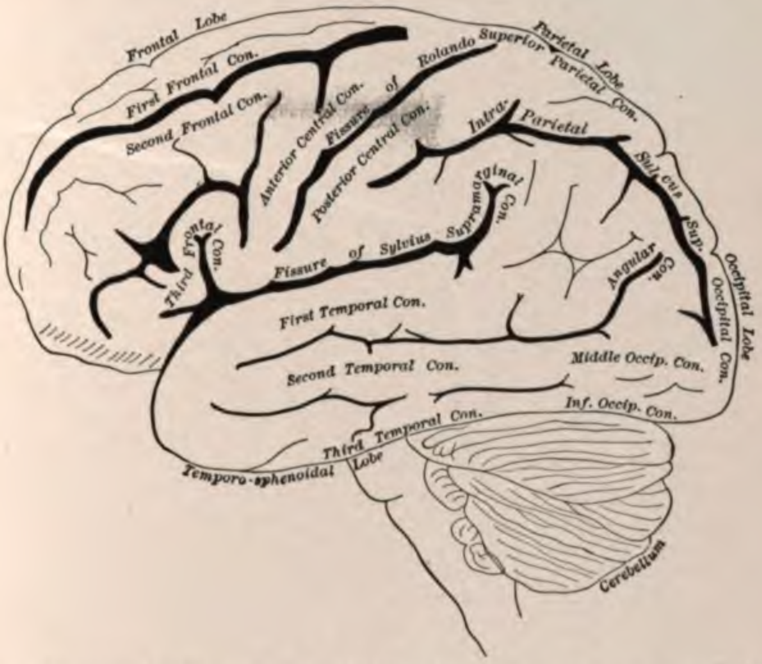


FIG. 289.—Diagram of the external surface of the left cerebral hemisphere of man, after Ecker.

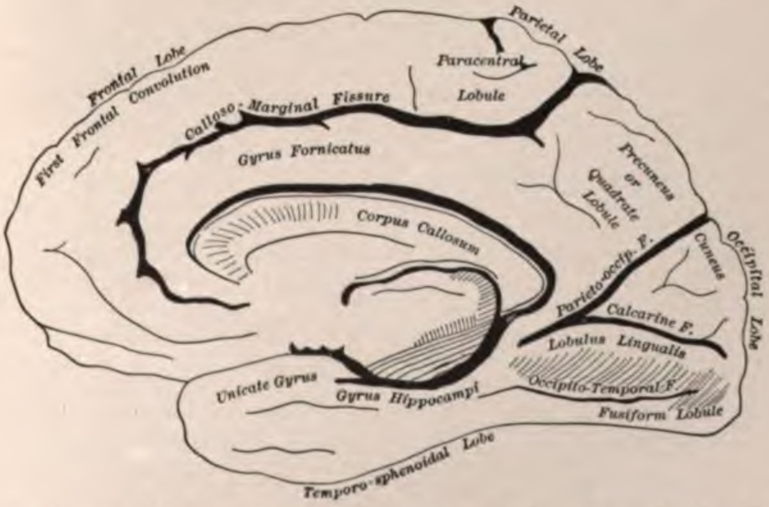


FIG. 290.—Diagram of the internal surface of the right cerebral hemisphere of man, after Ecker.

C. DIRECT AND CROSSED EFFECTS OF STIMULATION OF THE MOTOR CORTICAL AREAS

As already noted at page 632, the movements induced by stimulation of the cerebral cortex occur mainly in the opposite half of the body. But movements can be obtained also in the muscles of the same side. Of these *bilateral movements* some can be obtained even with a very weak stimulus. With the great majority of muscle groups, however, the movements on the same side can only be induced with relatively strong stimuli.

The *eye movements* are to be classed as bilateral movements since stimulation of one hemisphere causes both eyes to be rotated toward the opposite side. But the bilaterality in this case is only an apparent one; for the internal rectus of one eye contracts at the same time as the external rectus of the other. Inhibition of the antagonistic muscle is also an important factor. When all the nerves except the abducens to the eye muscles of one side, say the left, are cut in the monkey, the left eye naturally is deflected to the left, because the tonus has been destroyed in all but the external rectus muscle. But if movement of the eyes to the right is then induced by appropriate stimulation of the cerebral cortex, the left eye will turn back to the right as far as the median line even though the internal rectus has been paralyzed. That is, the stimulation has caused the tonus of the left external rectus to be intermitted. Since this experiment succeeds also when the corona radiata, the internal capsule, etc., are stimulated, the inhibition in question must be started from some center below the cortex (Sherrington, cf. page 636).

The action induced in the *face muscles* is really bilateral, although those of the opposite side contract the more powerfully. This is true of the buccinator as well as of the muscles of the tongue and vocal cords.

With regard to other muscular contractions induced from the same side of the brain, it is to be remarked: (1) that their latent period is longer than that of muscles on the opposite side (Franck and Pitres); (2) that they require a stronger stimulus; and (3) that the muscles of the same side of the body never make coördinated movements as do those of the opposite side, but show instead a tonic contraction more or less like an extended tetanus.

We see therefore that considerable differences exist between the movements of the same and of the opposite side, and, as Gotch and Horsley especially have emphasized, it is probably to be assumed that the muscles of the same side are not so immediately dependent upon the cortical areas as are those of the opposite side.

It is conceivable that the excitation is conveyed to the muscles of the same side by first crossing in the brain to the corresponding motor areas of the opposite hemisphere. But if this be the case, it is not the only course the excitation can take, for contractions on the same side have been obtained by a number of authors even after the removal of these opposite areas, or of the entire opposite hemisphere.

The crossing therefore must take place in the lower centers. Lewaschew obtained movements in the left hind leg by stimulating the left hemisphere after hemisection of the spinal cord on the left side. In this case the excitation had crossed to the right side of the cord and had crossed back again below the level of the section (twelfth thoracic segment) to the left half. But this does not teach us anything definite as to the part of the central nervous system in which the stimulus branches off from the main path to reach muscles of the same side. It is probable that this place is to be sought among the gray masses of the brain-stem. As Gotch and Horsley suggest, the cerebellum might have a large share in this distribution of impulses from the cerebrum.

D. THE COMMISSURES BETWEEN THE CORTICAL AREAS OF THE TWO HEMISPHERES

One would suppose *a priori* that the corpus callosum, the great commissure binding together the two hemispheres, must be of very great physiological importance; and, in fact, the most far-reaching hypotheses have been erected on this supposition. But the results of actual experiments designed to throw light on the purpose of this part are very meager. Several authors (Longet, Magendie, Flourens, Franck, Ferrier, Koranyi and others) have found that separation of the two hemispheres by a complete sagittal section through the corpus callosum produces no effect on the behavior of the animal (rabbit, dog) provided the hemispheres be left entirely uninjured. Lesions of the corpus callosum also produce no permanent effect (Wernicke). The necessary coöperation between the two hemispheres in the functions of the brain is therefore not brought about by the corpus callosum.

The fibers running in the corpus callosum from one motor zone to the other when stimulated from the upper surface of that body (except rostrum and the splenium) produce bilateral muscular movements. Applying the stimulus just behind the anterior genu gives movement of the head and eyes; applying it farther posteriorly we get in serial order: movements of the two arms at the shoulder joints, and of the upper half of the trunk; movements of the forearm, hands and fingers; movements of the posterior half of the trunk and of the tail; movements of the posterior extremities. No movements of the face muscles have been obtained. It was only very rarely that the movements were so isolated and so sharply localized as with stimulation of the cortex.

After extirpation of the motor zone on one side, the movements are unilateral; they are induced therefore with the help of the motor zone. When the corpus callosum is stimulated after sagittal section and after extirpation of one hemisphere, unilateral movements are obtained on the side from which the hemisphere has been removed. The excitation aroused by stimulating the fibers of the corpus callosum passes therefore to both motor regions and thence is propagated in the usual way to the nuclei of the motor nerves (Mott and Schäfer).

For the effects of sectioning the corpus callosum in cases of lesion of the cerebral cortex, see page 660.

E. CORTICAL EPILEPSY

It was observed by Fritsch and Hitzig in their early work on this subject that by continuous stimulation of the cerebral cortex of mammals, *cramp-like contractions* can be produced which do not remain confined to the set of muscles associated with the area stimulated, but may extend to all the

C. DIRECT AND CROSSED EFFECTS OF STIMULATION OF THE MOTOR CORTICAL AREAS

As already noted at page 632, the movements induced by stimulation of the cerebral cortex occur mainly in the opposite half of the body. But movements can be obtained also in the muscles of the same side. Of these *bilateral movements* some can be obtained even with a very weak stimulus. With the great majority of muscle groups, however, the movements on the same side can only be induced with relatively strong stimuli.

The *eye movements* are to be classed as bilateral movements since stimulation of one hemisphere causes both eyes to be rotated toward the opposite side. But the bilaterality in this case is only an apparent one; for the internal rectus of one eye contracts at the same time as the external rectus of the other. Inhibition of the antagonistic muscle is also an important factor. When all the nerves except the abducens to the eye muscles of one side, say the left, are cut in the monkey, the left eye naturally is deflected to the left, because the tonus has been destroyed in all but the external rectus muscle. But if movement of the eyes to the right is then induced by appropriate stimulation of the cerebral cortex, the left eye will turn back to the right as far as the median line even though the internal rectus has been paralyzed. That is, the stimulation has caused the tonus of the left external rectus to be intermitted. Since this experiment succeeds also when the corona radiata, the internal capsule, etc., are stimulated, the inhibition in question must be started from some center below the cortex (Sherrington, cf. page 636).

The action induced in the *face muscles* is really bilateral, although those of the opposite side contract the more powerfully. This is true of the buccinator as well as of the muscles of the tongue and vocal cords.

With regard to other muscular contractions induced from the same side of the brain, it is to be remarked: (1) that their latent period is longer than that of muscles on the opposite side (Franck and Pitres); (2) that they require a stronger stimulus; and (3) that the muscles of the same side of the body never make coördinated movements as do those of the opposite side, but show instead a tonic contraction more or less like an extended tetanus.

We see therefore that considerable differences exist between the movements of the same and of the opposite side, and, as Gotch and Horsley especially have emphasized, it is probably to be assumed that the muscles of the same side are not so immediately dependent upon the cortical areas as are those of the opposite side.

It is conceivable that the excitation is conveyed to the muscles of the same side by first crossing in the brain to the corresponding motor areas of the opposite hemisphere. But if this be the case, it is not the only course the excitation can take, for contractions on the same side have been obtained by a number of authors even after the removal of these opposite areas, or of the entire opposite hemisphere.

The crossing therefore must take place in the lower centers. Lewaschew obtained movements in the left hind leg by stimulating the left hemisphere after hemisection of the spinal cord on the left side. In this case the excitation had crossed to the right side of the cord and had crossed back again below the level of the section (twelfth thoracic segment) to the left half. But

Since the excitation in cortical epilepsy spreads to different muscle groups just the same after extirpation of the motor zone on the opposite side from the one stimulated, and since a single group of muscles is not absolved from the effect by extirpation of its own particular field in the cortex when the stimulus is applied to another, it is probable that the actual irradiation takes place through the mediation of subcortical centers. This is borne out also by the fact that once an attack is well advanced extirpation of the motor zone does not stop it.

F. SUPPRESSION OF THE MOTOR CORTICAL FIELDS

As the observations given in the preceding chapter have shown, the entire cerebrum can be removed not only from the lower vertebrates but from the rabbit and dog as well, without destroying the ability of the animal to carry out coördinated movements of locomotion. This proves at once that in these animals the motor regions of the cerebral cortex are not indispensable for movements of this kind. However, in the decerebrated dog there were noticeable disturbances in motion, which might not have been caused by removal of the motor region alone but also by the absence of other parts of the cerebrum. In order to establish the *physiological importance of the motor areas,* it is necessary therefore to study the behavior of animals from which these fields only have been extirpated.

When the motor fields of one hemisphere have been completely or mainly removed from a dog, for a time immediately following the operation there is a more or less profound disturbance in the movements of the opposite side; but this effect is only temporary. The animal gradually recovers its ability to move the opposite muscles, and after some time the motor defects become quite minimal. A dog from which Goltz removed the left hemisphere became "silly"; he was not so lively as before; did not play with other dogs, etc. But none of his muscles were entirely paralyzed. When he was called he came wagging his tail and let himself be stroked. When one started to go the dog followed. He fought off other dogs that displeased him. He held a piece of bread just as skillfully as a normal dog, but did not hold a bone so well with the opposite foot (the right) as with the other. He could stand up on his hind legs, although the right leg was somewhat weak. He ran here and there of his own accord, but turned oftener to the left than to the right. He could turn to the right, though less skillfully and less quickly.

It is therefore unquestionably true that a dog which has lost the motor zone of one side can still move those muscles which respond to stimulation of that cortical zone. It has been supposed that such an animal could not perform *intentional movements* with these muscles. But this view is controverted by the following observations on a dog whose entire cerebral cortex on the left side had been removed.

A bowl was placed before the animal containing bits of meat scattered in some coarse gravel. In scratching for the meat he used his left fore paw. But when this one was held fast he immediately made the same movement with the right fore paw (Goltz).

In a well-trained dog Gaule trimmed off on both sides all the cortex which could be visibly excited with a weak constant current. After the usual phenomena of paralysis had passed off, Gaule trained the dog again and was able teach him a whole series of complicated movements which gave evidence of his intelligence. However, he showed also a considerable number of disturbances of the motor mechanisms, among which may be mentioned especially his inability to perform isolated movements with only one extremity. Besides, his movements were excessive and were done with a waste of energy; and there was no proper gradation of them—e. g., in order to extend his paw, he was compelled first to sit upright and then to give both paws at the same time in a rather sudden and explosive manner.

From these and other experiments of the kind it appears that the movements of the dog, including those which must be regarded as intentional and conscious, can be carried out without the coöperation of the motor areas; but that on the other hand, the *finer regulation of these movements* is for the most part destroyed by extirpation of the corresponding areas. It would follow that in the dog the motor cortical areas are really necessary only for the nicer regulation of movements.

Horsley and Schäfer observed the following phenomena after extirpation of the cortical areas from the *monkey* (*Macacus*). If the whole excitable region on the convex side of the hemisphere were extirpated and only the median cortical region left, there was exhibited an almost complete paralysis of the opposite arm, paralysis of the facial muscles, weakness in the muscles of the posterior extremities, and a greater or less difficulty in moving the head toward the opposite side. The muscles of the trunk were unaffected, and the weakness in the posterior extremity was not so great that the animal could not use it in walking and climbing.

When only a part of the excitable region on the *convex surface* of the hemisphere was destroyed—e. g., the field for the wrist and fingers—a permanent weakness appeared in these muscles while the other muscles were movable in a perfectly normal fashion. In the same way destruction of the cortical field of the arm produced paralysis of the arm without any disturbance in the movements of the face, head, trunk or posterior extremity. When the destruction of the field was complete, paralysis of the corresponding muscles appeared to be permanent. But when a part of the field was left behind the ability to move the parts returned to a certain extent.

The consequences of destroying the motor region on the *medial side* are worthy of note. Following bilateral destruction of this region there was complete paralysis of the muscles of the trunk, a certain weakness in those of the arms and a very extensive paralysis in the muscles of the posterior extremities. The weakness in the arms involved mainly certain shoulder muscles, especially those which draw the shoulder blade upward and backward; it was less marked in the muscles of the arm and forearm, and scarcely or not at all noticeable in the finger muscles. Paralysis of the posterior extremities extended to almost all the muscles, only a few flexors of the hip joint being exempt.

By practice the monkey, like the dog, can acquire the use of muscles corresponding to the extirpated cortical fields; can learn, in other words, to execute *intentional movements* with them.

Hering, Jr., found that the cortical fields, electrical stimulation of which gave movements of the forearm, including grasping movements, could be entirely removed without destroying the animal's ability to close the fist on the opposite side or to use the hand in grasping objects.—Sherrington has made similar observations on the anthropoid apes.

Goltz had the opportunity of observing for more than ten years a monkey in which the greater part of the frontal and parietal lobes on the left side had been destroyed. Thus the motor region of the left hemisphere was entirely or almost entirely thrown out of function. Nevertheless, by practice the monkey succeeded in recovering his ability to use the right arm and right hand for definite purposes. He learned to grasp fruits with the right hand and to offer it in greeting, etc. He could move all of the muscles directly under control of the will, but the movements of the right limbs remained incomplete, cumbrous and awkward.

After these observations it scarcely ought to be longer assumed that the motor region in the monkey is of much greater importance than it is in the dog. It is indeed very probable that there is a difference in degree between the two, but certainly not a difference in kind.

Horsley and Schäfer's observations point to the interesting fact that in the monkey the motor cortical areas on the upper medial surface of the hemispheres are concerned mainly with what we may call the *coarser movements*, those by which the body is kept in its natural position and moves itself from place to place. The cortical areas on the convex surfaces of the hemisphere are of decidedly greater importance for the *more refined movements*, e. g., those which are executed by the muscles of the head, face and arms.

In order to establish the location and influence of the *motor cortical areas in the human brain*, we have recourse either to excitation experiments or to clinical and pathological observations. The former evidently can never be very numerous, and our knowledge of the functions of the human motor cortex rests mainly on clinical observations of the effects of lesions in the cerebrum.

It not infrequently happens that in post-mortem examinations very extensive lesions of the cerebral cortex are found, which were not accompanied in life by any observable disorder. Compilations of such cases, which we owe to Charcot and Pitres, Exner, Nothnagel and others show that these cortical fields which have no direct significance for the bodily movements embrace all parts of the cortex with the exception of the anterior central convolution inclusive of the operculum, the paracentral lobule, and the posterior part of the frontal convolutions. But if the lesions are found within the portions just named, a more or less extensive disturbance in the movements of the opposite half of the body is sure to have been observed. Hence we can say that the motor cortical field in man has on the whole the same extent as the cortical zone in the anthropoid apes, and that this covers the anterior central convolution inclusive of the paracentral lobule, and the foot of the frontal convolutions.

For working out the cerebral localization in detail the *very small cortical lesions* are of course the important ones. The more restricted the lesion, the more limited will be the disturbance of function, and of course the more definitely can the location of a particular field be decided upon. Such lesions have yielded results which agree essentially with the corresponding observations on the brain of the anthropoid apes, and with the excitation experiments on the human brain itself.

The disturbance in function which makes its appearance after a lesion in the motor region is as a rule greater at first than later, owing no doubt to some interference with the circulation and to *shock*. After this remote effect of the lesion has passed away, as it does within a few days, the primary loss of function comes more prominently to the front. Movements of parts connected with the cortical area destroyed can no longer be executed as before, and in adults they are either finally lost or are always thereafter executed with abnormal weakness. It is to be observed, however, that even such movements can continue to be performed in association with others. When, for example, the cortical field for the extension of the right thumb is entirely destroyed, the ability to make sure, strong and precise extensor and abductor movements with that thumb is lost; but in connection with the fingers it can still be used very skillfully in various kinds of complicated movements (v. Monakow).

The influence of the cerebral cortex in man on the movements of his body appears very clearly from the following observation. A patient was born with hemiplegia on the left side. When he was taken to the hospital at the age of twenty-nine, his left limbs were very much stunted. He could walk with the help of crutches, but could not lift his left leg from the floor. On opening the skull it was found that the whole right hemisphere of the cerebrum had disappeared and was replaced by fluid (L'Allemand).

In considering the *recovery of the muscular functions*, we must bear in mind that the extremities are represented not only on the convex surface of the cerebrum, but also on the medial side; also that according to observations on monkeys, it is only the coarser movements that are dependent on the latter region. When therefore the lesion occurs only on the outer convex portion of the cortex, it is still possible for the medial portion to direct the coarser movements of the extremities.

With lesions acquired very early in life, a very considerable degree of restitution is possible. In one case of defect of the two right central convolutions observed by v. Monakow, the patient at ten was able to use his left arm (atrophied though it was) in the proper way, in all possible sorts of manipulations—e. g., in playing ball; some considerable clumsiness was apparent however in the use of the left hand and fingers.

After a cortical lesion *contractures*—i. e., abnormal, persistent contractions—gradually make their appearance in the muscles of the paralyzed limbs. Different hypotheses have been put forward concerning the cause of these, but their discussion here would lead us too far afield. It must suffice to observe only that, according to H. Munk, contractures in the monkey can be prevented, if, as soon as the limbs affected begin to offer some resistance to passive movements, they be stretched as far as possible for a few minutes every day. The contractures are brought on by the loss of motility. Hence they do not occur in the case of animals which move about spontaneously after the operation, for the paralyzed extremity can be used in connection with the other extremities in walking even though isolated movements cannot be executed.

G. THE COURSE OF THE CONDUCTING PATHWAYS FROM THE MOTOR CORTICAL FIELDS TO THE NUCLEI OF THE MOTOR NERVES

The nerve paths which originate in the great pyramidal cells of the cerebral cortex proceed through the corona radiata to the internal capsule, through this to the crus cerebri and then continue distalward to the nuclei of origin of the motor nerves, with which they are connected. The *pyramidal pathways* are connected with motor nerves of the opposite side. The fibers belonging to the cranial motor nerves pass to the opposite side in different parts of the brain-stem, while the pyramidal fibers which reach the spinal cord cross for the most part in the medulla (crossed pyramidal tracts), but in part also in the spinal cord itself (direct pyramidal tracts). All these paths degenerate after destruction of the cerebral cortex (see Fig. 262, page 590).

Clinical evidence has shown that these paths pass through the corona radiata, forming, as we might expect, a pretty compact bundle. Lesions in the corona produce isolated paralyses of the face, arm or leg musculature, showing that the paths proceeding from the motor cortical areas are distinct from one another also in their further course.

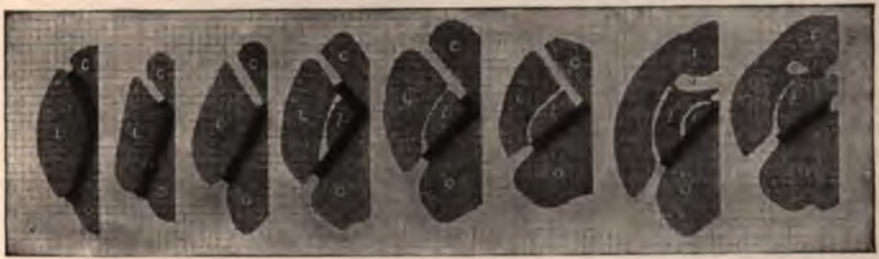


Fig. 292.—The motor tract (dark) at various levels of the internal capsule, after Beevor and Horsley. *L*, lenticular nucleus; *T*, optic thalamus; *C*, caudate nucleus; *a*, anterior commissure; *F*, point of junction of the lenticular and caudate nuclei.

In the internal capsule the pyramidal paths are drawn closer together, the deeper they go. According to Beevor and Horsley, at a high level they fill the entire cross section of the capsule with the exception of its most anterior and most posterior sections. Further down they are restricted more and more to the posterior limb of the capsule, as may be seen from Fig. 292.

The separate tracts can be fairly well stimulated in the internal capsule. Some responses are bilateral just as in the case of not overstrong stimulation of the cortex; but most are unilateral. The bilateral responses are: eversion of the lips, movements of mastication, swallowing, adduction of the vocal cords—all of them equally strong on both sides; opening and closing of the eyelids, protrusion of the lips, retraction of the angle of the mouth—all stronger on the opposite side; the rest are strictly unilateral.

Beginning at the most anterior part of the capsule which can be stimulated, and moving the electrodes gradually backward, the following responses in the order named are obtained in the monkeys (Beevor and Horsley): opening of the eyelids, turning the eyes to the opposite side, opening of the angle of the mouth, rotation of the head and eyes to the opposite side, rotation of the head alone to the opposite side, movements of the tongue, of the angle of the mouth, shoulder, elbow, wrist and fingers, thumb, trunk, hip, foot, knee, great toe and smaller toes (cf. Fig. 287). The points corresponding to the movements within any given cross section, however, are not sharply delimited, but overlap each other.

But the pyramidal tracts are not the only motor pathways from the cerebral cortex. According to Rothman, ablation of the pyramidal paths alone in the dog causes no essential change in the electrical stimulation of the motor region: the motor impulses are then conveyed by ***Monakow's bundle*** (see page 596). In monkeys however the latter plays but an unimportant rôle in this respect, for after section of the pyramidal paths, only movements of the hand, fingers and toes could be obtained by electrical stimulation of the cortex.

Even after complete suppression of all those pathways in the monkey, and notwithstanding the failure of subsequent stimulation of the motor region, the motor functions of the limbs were not permanently abolished. Impulses which reach the cord in *other ways* can always produce slight isolated movements of the fingers; indeed, after complete severance of all the paths of the lateral and anterior columns of the cord on one side, a restitution takes place which, while very incomplete, makes possible not only associated but isolated movements as well. There are therefore several pathways by which the cerebral cortex may influence the movements of the body.

H. DEVELOPMENT OF THE MOTOR AREAS OF THE CORTEX

The investigations of Flechsig on the formation of the medullary substance in the nerve paths of the central nervous system, have brought to light the fact that the pyramidal paths in man receive their medullary substance only at the very end of intrauterine life. In the dog these same paths are not provided with their medullary substance until after birth.

In accordance with this fact the excitability of the motor region in newborn dogs is but slight, so much so that it has been stated by some authors to be altogether wanting until the tenth day. This appears certainly to be incorrect, for Paneth has found, for example, that responsive movements can be obtained by stimulation of the cerebral cortex in dogs only one to two days after birth.

According to Bary, the first movements obtainable exhibit various noteworthy differences from those of somewhat older animals. They are not confined to separate groups of muscles as are the latter, but involve the whole anterior or posterior extremity of the opposite side; the duration of the contraction and the latent period are also much longer. Moreover, in very young animals the excitability of the cortex is easily destroyed by all sorts of injuries, narcosis, cooling, exposure, etc.

From about the tenth day onward special areas for the separate groups of muscles develop on the cortex, and *pari passu* with this development, the duration of the contraction and the length of the latent period become shorter, and the resistance of the cortex to fatigue also greater.

On the other hand it should be observed that in the guinea pig, in which the pyramidal paths receive their medullary substance *in utero*, the cortex is excitable before birth.

Of great interest also is the observation made by Herzen and others that newborn puppies from which the motor region was extirpated suffered no sort of motor disturbance, even immediately after the operation. This observation teaches us that at a time when the pyramidal paths are not complete anatomically, the motor region is incapable of any apparent physiological function, which is borne out also by the fact that puppies begin to support themselves on their feet only after the pyramidal paths have received their medullary substance.

§ 2. INFLUENCE OF THE CEREBRAL CORTEX ON THE VEGETATIVE PROCESSES OF THE BODY

In discussing the innervation of the different vegetative organs we have from time to time called attention to the influence of the cerebral cortex on their functions. In order to obtain a satisfactory conception of the cortical functions, it will be necessary to summarize briefly these and other similar phenomena in this connection.

Artificial stimulation of the cerebrum, as we have seen, produces an epileptic attack all too easily; and the excitation in such an attack is spread through the subcortical centers to all the cross-striated muscles. At the same time the respiratory, cardiac and vasomotor centers, the centers controlling the digestive apparatus and those of the iris, are also excited. But while this is of great interest, it gives us no definite information with regard to the probable normal influence of the cerebral cortex itself on these organs and their functions.

In similar experiments on *curarized animals*, the epileptic attack is masked because of the paralysis of the skeletal muscles, nevertheless the accompanying phenomena in the vegetative organs make their appearance as usual. But these experiments on curarized animals must not be trusted too far (Franck). It appears that the influence which is exercised by the cerebral cortex on the vegetative processes proceeds in general from the motor region and its immediate neighborhood. Indeed, Franck asserts that the effects which he has observed on respiration, the heart, blood vessels and salivary secretion in the dog after stimulation of the cerebral cortex can be obtained from almost the entire motor region, but from no other points on the cortex. Respiration is accelerated or slowed according to the strength of the excitation, just as in stimulation of the peripheral sensory nerves, and the depth of respiration is likewise affected. The glottis becomes narrow with the tendency to expiration and becomes wider with the tendency to inspiration, etc.—With weak stimulation the pulse rate as a rule is accelerated, with strong stimulation it is retarded. The blood vessels constrict. We know also that salivary secretion and contractions of the urinary bladder are influenced from the motor region (see page 239).

Other authors, however, have reached different conclusions. According to Horsley and Semon, the muscles of the vocal cords and of the larynx in the monkey have their cortical area in the lowermost part of the central convolutions and within this region the following definite movements can be localized: (1) bilateral adduction of the vocal cords; (2) the same movement, plus movements of the pharynx; (3) elevation of the larynx, accompanied by movements of the face, the jaws and the tongue; (4) depression of the larynx.

Spencer has obtained the following effects on the respiratory movements by stimulation of the cerebral cortex in several different species of animals (monkey, dog, cat, rabbit): slowing and stoppage of respiration by stimulation of the border of the temporal-sphenoidal lobe lateral to the base of the olfactory tract; acceleration of respiration by stimulation of the convex upper surface in the region of the motor areas; clonic inspiratory spasm (snuffing) by stimulation of the border of the olfactory bulb and tract, also on the uncinate gyrus.

Bechterew and Mislawsky make mention of a vasoconstriction from stimulating certain parts of the motor region, and a vasodilatation from other parts.[1]

From these observations it may be gathered that the cerebral cortex, especially the motor zone and its immediate neighborhood, exercises an *unmistakable influence on the vegetative processes* of the body.

Doubtless this influence is greater over some organs than over others. Movements like those of the larynx and to a certain extent also those of the thorax, which can be very exactly and very delicately graduated, especially after long practice, must naturally be very intimately dependent upon the cerebral cortex, even though the coarser movements of the same anatomical parts, such as are necessary for the mere ventilation of the lungs, are independent of the cerebrum. Quite different effects have been obtained from the cerebral cortex on the heart, blood vessels, etc. These effects, as has been repeatedly observed, are most correctly regarded as reflexes similar to those which are discharged by all kinds of afferent nerves. Most of them are accessory to the muscular movements controlled by the cortex, and some at least, like the acceleration of the heart and vasoconstriction, accompany every voluntary movement. The chief significance of this cortical influence on the circulatory organs is that they can be thereby adapted to the different requirements placed upon them. The effects of psychical states on the vegetative functions of the body, which have been discussed at page 577, are in all probability mediated by the cerebral cortex.

Finally, there are certain observations which indicate that different portions of the cerebrum have a different influence on the *general state of nutrition* of the body. Thus, if a large part of the most anterior portion of the dog's cerebrum be extirpated on both sides, the animal always exhibits a tendency to become lean and to remain so; he suffers very extensively also from a persistent inflammatory skin disease which is associated with great redness and itching. On the other hand, a dog deprived of its occipital lobe on both sides regularly becomes fat. It sometimes happens in this case that the dog acquires an eczema also, but it is much more easily held in check and much more easily cured (Goltz).

§ 3. THE SENSORY CORTICAL AREAS

The first method which we naturally think of in attempting to determine the significance of the cerebral cortex for sensation, is the investigation of effects upon the different sensations in man and animals which result from *lesion*, *destruction* or *extirpation* of different portions of the cortex. In experiments on animals, however, we meet at once with an obstacle in the fact that we can only judge of the probable loss of sensation by the movements and general behavior of the animal. Our conclusions are therefore very uncertain, especially in cases where the intelligence of the animal is greatly reduced. Since it is just such cases which ought to be most decisive for the purpose in hand, we are often forced to be content merely with finding that the animal's movements are *influenced* by some sensory stimulus, without being able definitely to say how far the action may be regarded as the expression of a conscious sensation, or whether it is not rather purely reflex. Our safest and most important conclusions, therefore, we get from observations on man.

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[1] For the effects of the cerebral cortex on the digestive organs, see pages 261, 264, 284.

We can obtain valuable information also by excitation experiments (of which more further along), by the action current, and especially by anatomical study of the afferent conducting pathways. In this section we shall limit ourselves to the study of regions where the sensory paths end. These regions are known as the *sensory areas—tactile area, olfactory area, auditory area, visual area*, etc.

A. AREA OF GENERAL SENSATION AND TOUCH

Since, as we have seen, even the complete removal of a whole hemisphere from a dog does not greatly inconvenience the animal, the locomotor movements being surprisingly little affected, it follows that the regulation of the coarser movements which goes on under the influence of the afferent nerves can be accomplished independently of the cortex. On the other hand, observations by Goltz, H. Munk, and others show that in the dog extirpation of the motor region and of the cortical areas lying immediately adjacent thereto causes all sorts of derangements of the tactile and the motor senses. It follows that the afferent pathways from all parts of the body serving the tactile and motor senses enter these regions. Similar sensory disturbances have been observed in the monkey also after extirpation of the motor region.

When the entire cortical area for the hinder extremity is removed, and as a consequence the muscles of the opposite leg can no longer execute finely graded movements, for some days after the operation there is complete insensibility in this extremity, and a certain bluntness of sensibility becomes permanent.

With still more extensive destruction, the finer movements of the hand and foot are permanently arrested, and for some time after the operation the sensitiveness of the paws is very much reduced, so that the animal reacts only to very painful stimuli. In fact the sensitiveness of the hand and foot becomes permanently so slight that a severe pinch produces no reaction at all (Mott). On the other hand, Schäfer has found that a monkey which does not react at all to a painful pinch immediately notices a very light tactile stimulus applied to the paralyzed extremity.

The monkey (page 645) from which Goltz had removed the entire motor region of the left hemisphere, took no notice of the gentle tactile stimuli applied to the right extremity. Stronger pressure stimuli, however, were always felt. The motor sensations were also somewhat diminished.

Although the *observations made on man* differ from one another in many points, on one point there is positive agreement, namely, that the motor region and its immediate neighborhood is the cortical area for the sense of touch. It is noteworthy that the motor and sensory disorders are not as a rule coterminous. In some cases the paralysis involves most of the muscles of the opposite side, whereas the disturbance in sensation going with it is of but slight extent; in other cases with a sharply circumscribed motor paralysis, there goes a reduction of sensibility covering a very considerable area.

From the summaries of *clinical cases* of this character it appears with perfect definiteness, however, that so far as these particular disorders are concerned, lesions of the occipital, temporal, and the greater part of the frontal lobes are of no consequence; that therefore the cortical field, lesion of which is accompanied by loss of general sensation and touch embraces the central and parietal convolutions, the paracentral lobule and possibly the posterior part of the frontal convolutions.

More detailed study of cases appertaining to this subject appears to show further that the anterior central convolution, the importance of which as a place of origin for the long-fibered efferent tracts was discussed at page 633, can be thrown out of function without entailing any loss of general sensation, that therefore the sensory cortical area consists for the most part of the posterior central and the parietal convolutions. The disturbances to the different modalities of sensation resulting from lesions within these parts of the cortex appear to be rather different in degree. The pain sensations suffer least; the pressure and temperature sensations are said to be somewhat reduced, but are not by any means always abolished. The power of localization is very profoundly affected and the patients make very great mistakes when tested for this sense. The motor sensations are likewise much disturbed; patients can neither recognize the exact position of their limbs nor tell when they are moved passively. Whether there is any dependence of the modality affected upon the exact place of the lesion within the general region, we cannot say definitely at present.

Further proof of the functional relations here indicated is found in the *anatomical discoveries* concerning the convergence of the conducting pathways of the tactile and other general sensory nerves into the cerebral cortex. As Flechsig has pointed out, these for the most part enter the posterior central convolution and only a small fractional part of them reaches the anterior central. Besides, the paracentral lobule, the first frontal convolution and the gyrus fornicatus also receive such fibers. But, on the other hand, the origin of the pyramidal pathways is found chiefly in the paracentral lobule, in the whole anterior central convolution and in the posterior part of the first frontal convolution. It is significant also in view of this arrangement that the anterior central convolution, as well as the posterior part of the first and second frontal convolutions, has a different structure from that of the other cortical regions and that of the posterior central convolutions. The chief difference consists in the enormous thickness in the former of the layers of the middle-sized and the superficial giant pyramidal cells (Cajal, see Fig. 284). From these relations we can understand how it is that motor paralysis of cortical origin is not necessarily accompanied by loss of sensibility.

It is also possible to convince oneself by stimulation that the region under consideration is in fact a terminus of sensory nerves. If the central convolutions of an unæsthetized man be stimulated electrically, while he feels no pain there is at first an itchy, prickling sensation in that part of the body whose muscles contract to the stimulus—an observation which agrees with the statements of patients suffering from cortical epilepsy regarding the premonitory symptoms of epileptic attacks.

In short, from the clinical evidence obtained on men and from experiments on animals it appears that the cortical area of the general sensory and tactile nerves is very closely related to the motor cortical field in a spatial sense as well as in a functional sense, but that in man it lies, at least for the most part, outside the motor cortical field (Fig. 293).

B. THE CORTICAL AREAS OF TASTE AND SMELL

The parts of the brain directly connected with the olfactory organ are very differently developed in different genera of animals. In man, as we have already seen (page 486), this sense is but slightly developed.

Our knowledge of the cortical areas of the *olfactory nerves* is based almost exclusively on *anatomical evidence*. Judging by this, the olfactory area in man embraces the whole posterior edge of the base of the frontal lobe and the basal part of the gyrus fornicatus on the one hand and the uncus and a part of the neighboring inner apex of the temporal lobe on the other. These two areas are connected at the base of the insula (Fig. 294).

Speaking of the cortical area for the *gustatory nerve*, Bechterew states that in the dog bilateral destruction of a region corresponding to the anterior lower portion of the third and fourth external convolutions (Fig. 282) obliterates the sense of taste entirely; with unilateral destruction there is total loss of taste on the opposite side and a slight weakening on the same side as the lesion. Following only slight injuries, an improvement is noticeable within a few days, while after more extensive lesions the defect continues for months. Stimulating these portions of the cortex, Bechterew noted contraction of the lips on the opposite side, movements of the tongue, movements of mastication and swallowing.

C. THE AUDITORY AREA

H. Munk finds that removal of the temporal lobes on both sides produces complete deafness, but no other disturbance. Extirpation of one temporal lobe makes the animal deaf in the opposite ear. Stimulation of the temporal convolutions produces movements of the external ear which are probably connected in some way with auditory impressions.

Similar results have been observed by other authors, but we find it stated by still others that bilateral extirpation of these parts produces only temporary deafness or no evident sign of it at all. Brown and Schäfer completely removed both temporal lobes from a monkey. Immediately after the operation the animal's intelligence was very much affected, but this condition gradually passed away so that the animal once more became very intelligent. The authors themselves and several other physiologists and physicians tried numerous experiments with the animal and came to the conclusion that all its senses including hearing were perfectly acute. Moreover, there was no chance for the claim that the reactions of this animal to auditory stimuli were really due to excitation of the cutaneous nerves. From these observations it appears therefore that the auditory pathways do not end in the temporal lobes alone, although they may be most concentrated there.

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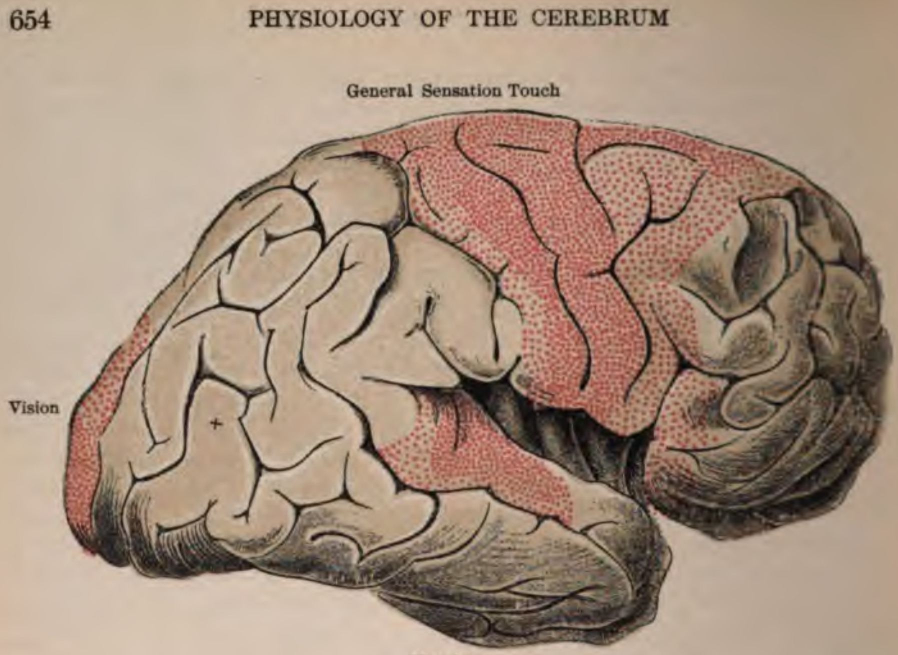

FIG. 293.—Right cerebral hemisphere seen from the outside, after Flechsig. In this and the following figure the sensory areas are indicated with red dots. The region where the dots are thickest is the region where most of the sensory pathways end.

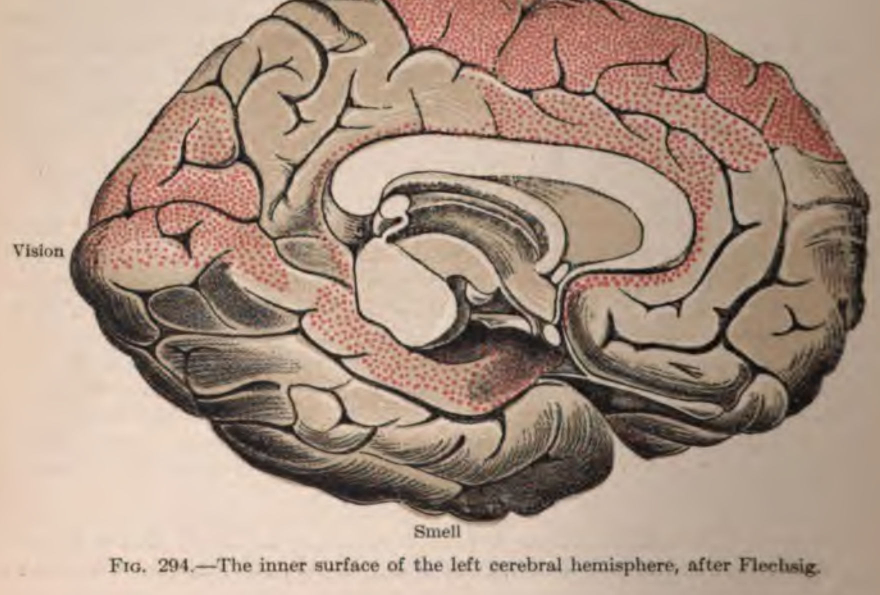

FIG. 294.—The inner surface of the left cerebral hemisphere, after Flechsig.

the auditory nerves. The fibers of this nerve leaving the ganglion cells of the cochlear nucleus are carried by the lateral fillet to the posterior quadrigeminal body (Flechsig and Bechterew). This is abundantly connected with the internal corpus geniculatum, which in turn is connected exclusively with the cortex of the temporal lobe (v. Monakow). According to Flechsig, the two transverse convolutions of this lobe represent the substations of the auditory nerve.

These convolutions lie deep in the fissure of Sylvius, where they push in between the posterior border of the *island of Reil* and the outer free surface of the first temporal convolution. The fact that in all cases of total deafness as the result of bilateral destruction of the human cortex thus far known, this region of the two transverse convolutions was affected, speaks strongly for its importance as an auditory cortical area. Cases of deafness or of dull hearing on one side following injury to this region, or to its coronal radiation or to its fibers in the internal capsule, furnish evidence to the same effect.

D. THE VISUAL AREA

Experimental as well as *clinical* and *anatomical* evidence indicates that the cortical area for the optic nerve is to be sought chiefly in the occipital lobe. Statements differ a great deal as to the exact boundaries of this area, owing in part at least to the fact that in some animals the localization is sharper than in others.

In the *dog*, according to H. Munk, the two retinæ are projected upon the occipital lobes in the following manner. The extreme lateral part of each retina is represented by the extreme lateral surface of the occipital lobe on the same side. But by far the greater part of each retina is represented by the remaining greater part of the occipital lobe on the opposite side, the inner edge of the retina corresponding to the median edge of the occipital lobe, the upper edge of the retina to the anterior edge of the lobe, and the lower edge to the posterior edge.

As opposed to this Goltz, among others, has observed after bilateral extirpation of the occipital lobe, that while a great reduction of the visual power and a very considerable loss of intelligence may result, the animal still cannot be called totally blind. For, although he may not respond to a threat with the hand or with a light, he still is able to avoid obstacles fairly well without being guided in any way by the sense of touch. These observations show that the animal in this very low mental condition either receives visual sensations through the remaining parts of the cortex, or that the movements can be regulated by retinal impulses with the help of the subcortical centers.

Several authors, however, have observed that in the dog a temporary reduction of the visual power on the corresponding halves of the two eyes (homolateral hemiamblyopia) may result from the removal of other cortical regions (e. g., the motor zone). One would be inclined to conclude from this that while most of the fibers from the optic tracts reach the occipital lobe, some of them have termini in other parts of the cortex. But the following observations by Hitzig, which have recently been confirmed in their entirety by Exner and Imamura, prove that the relationship is still more complex. If a part of the occipital cortex be removed from a dog, and then after the hemiamblyopia has disappeared the motor zone also be removed, no additional effects on vision are produced. But the remarkable thing is that the same is true if the operations be performed in reverse order. After the hemiamblyopia resulting from removal of the motor zone has passed off, an extirpation within the occipital lobe is entirely without effect. We shall discuss the significance of these facts further along (page 660).

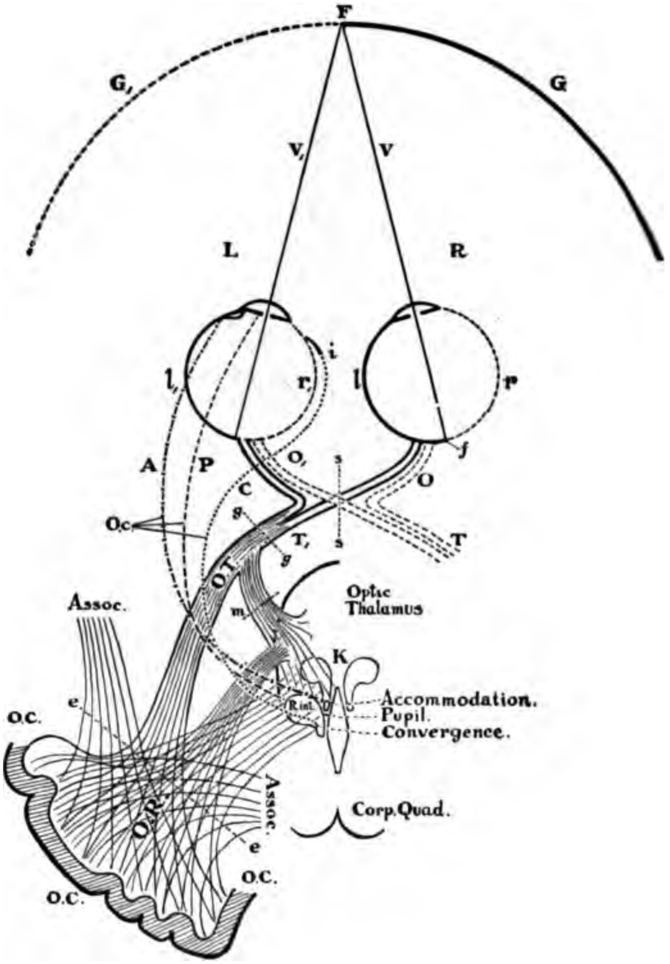

FIG. 295.—Schematic representation of the optic tracts, modified from Fuchs.

Division of the optic tract at *gg*, or *cc*, or removal of the left occipital lobe produces right hemianopia. In the first case there would be no reaction of the pupil to light on illuminating the left half of either retina. Division of the chiasm at *ss* produces temporal hemianopia. Division of the fibers at *m* abolishes the reaction of the pupil to light. The fibers connecting the optical cortex (O.C.) with the midbrain (cf. page 657) and with other portions of the cortex (Assoc.) (page 660) are shown. O.R., optical radiation; O.c., oculo motor nerve.

In the *monkey* the observations of H. Munk, Brown and Schäfer and others agree in showing that extirpation of one whole occipital lobe results in loss of vision on the corresponding halves of the two retinæ (homolateral hemianopia, Fig. 295), and bilateral extirpation in total blindness. According to H. Munk, there should be a projection of the retina upon the occipital lobes of the monkey like that described above for the dog. But Brown and Schäfer have not obtained any positive results in this direction by partial removal of the occipital lobes.

The *clinical evidence* is perfectly clear that in man the cortical area for the optic nerve is situated in the occipital lobes. A sufficiently extensive lesion of the occipital cortex is followed just as in the monkey by homolateral hemianopia on both sides. As a rule, this is not complete, for the line of separation leaves the central part of the visual field intact. In certain individual cases of bilateral hemianopia accompanying lesions of both occipital lobes, the portion corresponding to the yellow spot may remain entirely free.

Opinions differ considerably as to the exact *location of the visual area* in the occipital lobe. According to Nothnagel, it is coterminous with the cuneus and the first occipital convolution; according to Vialet, with the whole median surface of the occipital lobe. Still others extend it further, to the first and third occipital convolutions, or even to the angular gyrus, which latter, according to Ferrier, is the region for distinct vision. As opposed to these, and on the strength of some very convincing cases, Henschen in particular advocates the view that only the cortex along the calcarine fissure is to be regarded as the area of vision.

Flechsig, on the basis of his embryological studies, takes very much the same view. Most of the optic fibers end in the wall of the calcarine fissure, and those regions of the visual area situated outside of this limited tract have but a limited share in the true visual process.

The *visual conducting paths*, according to most investigators, take the following *course* to the occipital cortex. The optic fibers springing from the ganglion cell layer of the retina pass to the chiasm; those corresponding to the outer lateral parts of the retina remain uncrossed; the remainder cross. With their end arborizations some come into relation with the ganglion cells of the anterior quadrigeminal body; many more, and among them the fibers from the macula, with the cells of the external corpus; and a smaller number with cells in the pulvinar. New pathways spring from these various cells and make their way to the occipital lobes.

In the opinion of v. Monakow, the reason the macula region so often remains intact in cerebral lesions is that it is probably represented throughout by a rather extensive cortical zone; the macula fibers then would be connected with practically all parts of the corpus geniculatum ext.; consequently, if the lesion left any fibers to the cortex intact, impulses from the macula could still be transmitted.

According to Flechsig, efferent fibers pass out from the occipital lobes, and convey impulses from the cortex to the optic thalamus and the anterior corpus quadrigenum by way of which impulses can be conveyed from the optic lobes to various muscles and other peripheral organs.

Artificial stimulation of the cortex back of the angular gyrus in the monkey (H. Munk, Schäfer) gives conjugate movements of the eyes toward the opposite side, the plane of vision being at the same time directed upward, downward or horizontally, according as different points of this region are stimulated. The latent period of these movements is longer than that of corresponding eye movements which appear on stimulation of the frontal lobe, they are also obtained after removal of the frontal lobe; hence are probably evoked through the above-mentioned subcortical centers. The same movements occur when the occipital cortex and the eye region of the opposite frontal lobe are stimulated simultaneously.

Movements of the iris also can be aroused by stimulation of the cerebral cortex. Dilatation of the pupil is most easily obtained in the monkey by stimulation of the motor region for the eye muscles and of the occipital lobe. This dilatation appears when the cervical sympathetics are cut, and probably must be regarded as at least partly due to an inhibition of the sphincter muscle. Constriction of the pupil seems to be obtained only as an exceptional result of cortical stimulation.

E. RECAPITULATION

From the facts which have just been brought forward with regard to the *cortical areas of the nerves of special sense,* it appears probable that they, like the motor areas, *become more sharply concentrated the higher we ascend in the scale of mammals*; also that their importance for special sensations becomes greater and greater. Moreover, it is evident that, as a general rule, efferent paths from all the sensory cortical areas are so arranged as to convey impulses to just those muscles which are of the most service to the particular senses. Thus, the cortical field for the sensory nerves of the skin, of the muscles and the joints lies in the immediate vicinity of the great motor cortical area or practically coincides with it; we get movements of the ears from the temporal lobes where lie the auditory areas, and movements of the eyes from the occipital region. We shall discuss the deeper physiological and psychological significance of these cortical areas in the following section.

SECOND SECTION

THE PSYCHO-PHYSICAL FUNCTIONS OF THE CEREBRUM

While an exhaustive discussion of the *psychical activities* of man is plainly out of the question in this book, a brief summary of the most important facts of modern physiological psychology seems called for here, because, quite independently of any particular psychological system, or of any spiritualistic or materialistic point of view, these facts may of themselves afford us valuable insight into the complex mechanism of cerebral activity. We designate these functions *psycho-physical* in order to expressly indicate that we shall discuss them not from the standpoint of metaphysics, but solely from the standpoint of physiology, and without wishing to take any position with reference to spiritualism or materialism.

§ 1. THE SIGNIFICANCE OF THE MOTOR AND SENSORY CORTICAL AREAS

We have seen that the motor cortical areas constitute the place of origin of the long-fibered motor pathways, and that the sensory pathways terminate in different cortical areas. What then is the physiological and psychological significance of these areas?

Theoretically, the simplest psychical events probably take place in the cortical areas of the higher senses, for in such events the bodily movements play but a relatively subordinate part, or at least do not occupy so prominent a place in consciousness as do the sensory components of our experiences. We shall therefore begin with the sensory areas.

The conception most widely held at present is, that the *excitation of these cortical fields* itself produces the appropriate simple, special sensations; that the simple visual sensations, for example, arise in the visual area of the occipital lobe; the simple auditory sensations in the auditory area of the temporal lobe, etc.

But this cannot be looked upon as actually proved. If, for example, we follow in our imagination the conducting pathway of optical impressions from the periphery to the cerebral cortex it is evident at once that any complete interruption of that pathway, no matter where it might occur, would cause total blindness; also that any partial interruption, wherever it might occur, would necessarily produce partial blindness. From this point of view it is a matter of indifference whether the interruption take place by a peripheral lesion or by a lesion in the corresponding part of the optical cortex. If only we can assume that the activity of any part of the cerebrum, be it never so small, will occasion a conscious process, then one can say that the simplest visual impression is produced by excitation of the optical area in the cortex. But this is only an unproved postulate.

Moreover, our simplest conscious states are always very complicated. With the simplest optical impression—that, for example, of a luminous point—we observe not only the strength of the light and the color, but its position in the field of vision, its apparent distance from the eye, its apparent size. All this is given at the first glance, and it is at least very difficult to suppose that all this can come into consciousness by the activity of the optical cortex alone.

It would appear to be justifiable therefore to assume that pathways pass out from the optical cortex and connect this field with others, and that even the simplest visual sensations require the coöperation of several different cortical regions. The excitation furnished the optical cortical area is of course an important, perhaps the most important, component of the whole process. And with Flechsig we would especially emphasize the point that what gives the sensation its active character, what makes it essentially clear and distinct, is brought about by this very component.

The manifold ways in which the *different sensory areas are connected together* and the great importance of such connection for the objective valuation of our sense impressions are beautifully illustrated by the following observation on successfully operated patients born blind. Such persons learn to recognize an external object presented to them by feeling it with the fingers

—i. e., the visual impression gets its proper interpretation through the idea already gained by touch. But if the patient has seen in this way an object a single time, he is able to recognize it immediately with the eye the next time. The connections of the optical center with the other parts of the cerebral cortex were therefore already present, and it was only necessary for the patient to compare the visual impression with the tactile impression a single time in order to fix the memory picture of the object permanently. It can scarcely be maintained therefore that the optical memory pictures are, as has so often been assumed, so to speak imprinted on the optical cortex, for in cases like these just described there would not be time enough to form such an imprint.

The exhaustive analysis which Exner has made of the visual disorders observed by Hitzig following lesions of the motor cortex in the dog (cf. page 655) shows that different cortical fields participate in the perception of things visually. When the cortex within the motor region is destroyed, many fibers which connect the occipital lobe with this region are severed. Hence the perception aroused by appropriate stimulation of the optic nerve will be wanting in those components which relate to motility. Consequently the elaboration of the visual impression after the operation becomes deficient and hemiamblyopia sets in, notwithstanding that the optical cortex is intact. Recovery from the visual disorder is possible because the hemisphere of the opposite side takes up the functions of the injured side, connections being gradually established which lead ultimately to complete restitution of function. Extirpation within the occipital lobe of the injured hemisphere now is without effect because this hemisphere has no further part to play in the elaboration of visual impressions.

This interpretation receives substantial support from the fact that section of the corpus callosum—which in an injured animal is without demonstrable effect (see page 641)—in a dog which has already lost the motor zone and has recovered from the resulting hemiamblyopia, immediately produces this disorder again and leaves no possibility of recovery. Likewise the hemiamblyopia continues permanently if one removes a piece of the cortex and at the same time sections the corpus callosum.

What has here been said of the visual area is of course true for the cortical areas of the other higher senses, and for those of general cutaneous sensation, touch, etc.; the excitation immediately aroused is conveyed by means of new pathways to other parts of the brain, and by the coöperation of several different cortical fields the conscious process associated with those particular senses is aroused.

From all that we know of the central organs of the nervous system, it appears very probable that the *motor cortical fields do not of themselves originate the impulses* which they send to the muscles of the body, but that they must first be acted upon by other cortical regions. We naturally think first of the closely associated sensory cortical region as a source of such excitation, and it cannot be denied on purely *a priori* ground that in very many simple movements aroused by the cortex, the efferent impulse is discharged by an afferent impulse very much after the manner of a reflex. Here belongs the touch reflex, for example, described by H. Munk, which consists of a feeble flexion of the toes and the foot, when the hairs on the back of the foot are lightly stroked the wrong way, and which is permanently lost after extirpation of the cortical region corresponding to the extremities. This mechanism, however, does not suffice for complicated movements, and still less for learning new movements. In such cases several other portions of the cortex must be called into play and it is these which finally stimulate the discharging cells of the motor pathways.

This conclusion is supported by the circumstance that in localized artificial stimulation within the motor cortex (provided no epileptic attack is induced) the movements obtained are always relatively simple, being confined to a few groups of muscles. They almost always lack the orderly coördination of several different groups which characterize the voluntary movements, and even appear in certain reflexes from the spinal cord (see page 587).

The following observation may be cited as still further support for this conception. If the cortical area of a definite part of the body be sought out by electrical stimulation, and it be then isolated from the rest of the cortex by a circular cut, the effect is just the same as if it were extirpated in toto, although the blood supply may not have been disturbed by the process of cutting (Marique, Exner, and Paneth).

The following experiment by J. R. Ewald likewise speaks against the idea that the voluntary motor impulses originate in the motor cortical areas. A small hole is made in the skull of a dog and after opening the dura mater, electrodes are fastened in in such a way that the cortex can be stimulated as the animal moves freely about. Different movements can then be induced according as one or the other of the cortical fields is stimulated; but the animal takes no notice of them, even when just in the act of making a voluntary movement. It is clear that such a stimulus does not interfere with the normal stimulus, which, it would seem, therefore, must originate elsewhere.

§ 2. LANGUAGE FACULTIES

The ability to use language, as even a cursory survey of the way in which we acquire the power of speech will show, requires the coöperation of a number of different parts of the cerebral cortex. Lesions in different parts of the cortex and of the corona radiata produce various disorders in the language powers, the study of which will give us further insight into the mechanism concerned in psychophysical processes. What follows is based mainly on the ideas of v. Monakow.

A child is born with the ability to move all his muscles; he sees and hears. But he lacks for the most part the power to coördinate his movements to any purpose: he does not understand what he sees, he does not comprehend what he hears; he has " no language but a cry." But his power to see and to hear begins to be exercised. He gradually learns to recognize people and the commonest objects about him, he hears the names by which these people and things are called and learns little by little to recognize them. Finally, he begins to imitate these sounds and after many fruitless attempts succeeds at last in compassing the first intelligible and orderly articulate sound. This is usually the name of his mother.

And so it goes on. The child gains wider knowledge from the appearance of different objects, learns their names and practices them—i. e., learns to make the necessary movements of his organs of speech.

Soon the ability to form *ideas* is developed, by which we mean that the child learns to include the single concrete objects of the same kind under a common designation. And as his mental powers develop still further, he comes to incorporate into his circle of ideas notions concerning the relations of objects to one another, notions of their properties, their position in time and space, etc. Finally, the abstract ideas also begin to be more than mere words for the child, and a view of the world, as yet of course very vague and indefinite, becomes his own.

In all this course of development of the mental powers, *speech* plays a determining part and this part becomes more significant the more the child comes to rely upon abstract ideas. He requires no great store of words to represent objects themselves and their simplest relations to each other, for direct contemplation will serve him here. But when it comes to more complicated relations of concrete objects, and especially to abstract ideas, a satisfactory conception can only be gained through the medium of language.

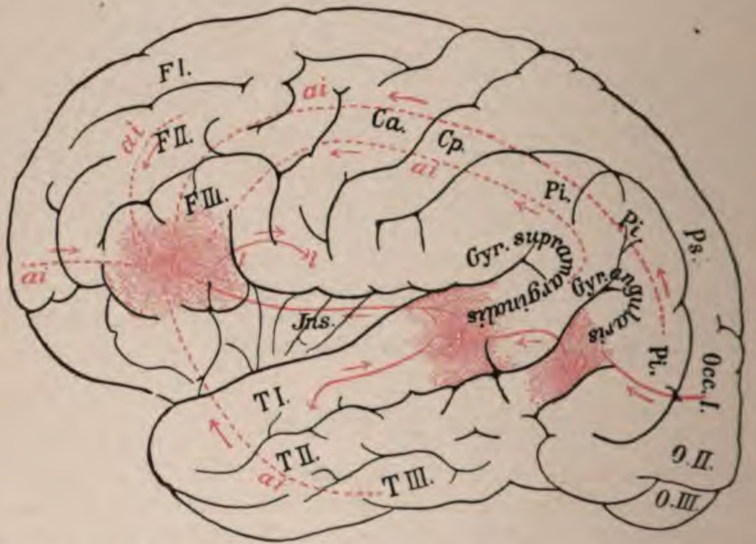

Fig. 296.—Diagram of the speech tract together with the various centers of the cerebral cortex concerned in speech. *L*, area of the image of speech movements; *A*, area of word-sound memory; *O*, area of memory for the optic images of writing; *Occ.I.*, *O.II.*, *O.III.*, first to third occipital convolutions; *F I.*, *F II.*, first and second frontal convolutions; *F III.*, third frontal convolution (Broca's area); *T I.*, *T II.*, *T III.*, first to third temporal convolutions; *Cp.*, posterior central convolution; *Pi.*, inferior parietal gyrus; *Ins.*, island of Reil; *ai*, association tracts between *L* and the central portions of the association areas; *Li.*, motor speech tract.

The names of *concrete* objects have therefore much less significance for our mental operations than the words by which we designate *abstract* ideas, and we may conclude from this that the latter require a more complex order of activity on the part of the brain than the former. Accordingly we find in certain disorders of speech resulting from injuries in the brain—e. g., in lighter forms of the so-called amnestic aphasia—that the patients forget proper names and the names of things, while abstract substantives, verbs, adjectives, conjunctions, etc., are retained.

The language faculties make a distinct advance when the child learns to read and write. The symbols of spoken words used in written language—words and the letters of which they are composed—are inculcated in the same way as spoken words, and at the same time the ability is acquired to reproduce these symbols in writing. The movements used in writing, just like other movements, are controlled by various afferent impulses.

Our powers of language are made up therefore of the following components: (1) Memory pictures of the written and spoken words; (2) the ability to make the coördinated movements necessary in speech and writing; (3) constant control of this ability through various afferent pathways.

Lesions in certain regions of the cortex or in the corona radiata produce disturbances of greater or less extent in these delicate mechanisms, which are comprehended under the name of *aphasia*, and differ in kind and extent according to the place of lesion.

One of the simplest forms of aphasia is that of *alexia*, or *word blindness*, which is characterized by the inability to recognize written or printed letters or to compose words of them. This disorder (in right-handed people) follows injury to the white matter of the left angular gyrus and of the second occipital convolution, the corresponding cortex remaining uninjured. Simple alexia would thus be produced by interruption of the association fibers connecting the visual cortical area with other cortical regions which are active in the use of language. When the cortex alone of the angular gyrus is affected, alexia does not ensue, and this may be taken as a proof that that portion of the cortex is not, as has been supposed by many authors, the " center " for reading.

Alexia may occur without affecting the ability to speak, and this is readily understood when we remember that aside from writing reading is the latest acquirement in the development of the language powers, and might well exercise but a slight influence on the speech mechanism pure and simple.

It is possible for the patient to be able to write even when he cannot read, and this is explained by supposing that the association pathways which are active in writing have escaped the lesion. Such a patient may even succeed in deciphering script or printing by executing the appropriate movements for making the letters which he sees, but would not otherwise comprehend. In this case he reads by using the memory pictures of these movements and by bringing them through association fibers into connection with the cortical areas which mediate the necessary movements of the organ of speech.

Other disorders of the language powers are produced by lesions within the red area in Fig. 296, and the white matter lying immediately under it. In right-handed people it is always the left hemisphere which is affected. These disorders differ both in kind and extent, and can be divided into two groups—motor and sensory aphasia—according as the expressive or the perceptive phase of language is the more affected. Between the two are various intermediate modifications.

Motor aphasia, which through the work of Broca has been of so much importance for the development of our views concerning the functions of the cerebrum (see page 631), appears in its purest and simplest form when only the special motor functions of speech are arrested. In this case the person affected can write and can understand written or spoken words normally, but cannot speak or read aloud either voluntarily or after another person. The part affected is only the subcortical portion beneath the posterior third of the third frontal convolution. The lesion interrupts only the conducting pathways serving the organs of speech, on their way to the internal capsule.

But if the cortex of the posterior part of the third frontal convolution (Broca's convolution) is injured, other disorders appear even though the lesion be a very slight one. The patient now loses, besides the power of speaking, the power of writing spontaneously, although he may acquire it again. The ability to write by dictation is always partially destroyed soon after the lesion makes its appearance.

More profound still are the disorders when the third left frontal convolution is somewhat more extensively injured. Writing spontaneously and by dictation becomes very difficult, although the defect is not due to any motor effects on the right arm. It is difficult for the patient to understand written or printed words even though he may recognize them perfectly; he quickly tires of reading, and cannot compose words when the proper letters are shown him one after the other, cannot recognize words when the letters are placed vertically instead of horizontally, etc. On the other hand, the ability to understand spoken words and to copy words in writing is generally unimpaired.

When the superior temporal convolution is injured somewhat extensively, the other typical form of aphasia appears. This is called, from its most prominent symptom, *word deafness* or, after Wernicke who first described it, *sensory aphasia.*

This form of aphasia may also be very simple in character: the patient can speak, read and write; his comprehension of language is undisturbed, but he cannot understand spoken words, whereas he can not only hear but also correctly interpret every other kind of noise and sound. He lacks the ability to interpret the sounds of letters; and this is probably due to the interruption of certain association pathways, the elements serving other language faculties remaining unimpaired.

As a rule, however, word deafness is closely associated with much more serious disorders. This is what we should expect, if we remember how great is the influence of spoken words on the total language powers, and how numerous are the connections of the auditory association pathways with other parts of the brain. Any cortical lesion in the temporal lobe must therefore necessarily involve many different bundles of association fibers; consequently word deafness is accompanied by many different effects on the general language powers.

Clinical observations have given us the following facts with respect to this form of aphasia. With lesions in the posterior part of the first temporal convolution, voluntary speech appears on superficial examination not to be particularly affected, but in reality it is always paraphasic—i. e., the person shows an inclination to confuse words and to talk gibberish; and since the auditory control is largely impaired he makes all sorts of errors in enunciation without being aware of them. Repeating words after another person is for the most part impossible, because the sounds of words are not retained long enough in the memory to be understood. Reading aloud is out of the question, because, while the letters are seen, they are not always recognized as signs of certain definite sounds. The ability to write spontaneously or after dictation is very profoundly affected and the ability to copy is often somewhat reduced. We find likewise when the destruction is somewhat more extensive that it is always difficult and sometimes impossible for the patient to understand writing.

The disorders which are produced by lesions of the first temporal convolution may vary also according to the mental and literary culture of the individual. Highly educated persons suffer less in their ability to understand written or spoken words or in their ability to write than do the uneducated.

Recovery of language powers lost by these various lesions is to a greater or less extent possible. This is explained in part by the assumption of the lost functions by the right hemisphere, and in part possibly by the establishment of new associations by means of collateral and other connections which have been left unharmed.

When the language powers are destroyed to any great extent, the mental powers must naturally suffer. Here again the extent and duration of the disorder will depend upon the position and extent of the lesion as well as upon the relative importance of the different components in the person's particular language mechanism. If, as is usually the case, the individual is influenced most by the sound images of words, word deafness would naturally produce a greater reduction in his intelligence than if he relied mainly upon memory pictures of printed or written words.

Closely related but not identical with the *language faculties* are the *musical faculties*. Music constitutes a language of its own, the finer nuances of which are intelligible only to a relatively few favored individuals. Clinical observations made within recent years have shown that brain diseases may cause disorders in these powers exactly similar to those affecting the ordinary language faculties. Thus we find loss of the ability to sing (vocal motor aphasia), note blindness, loss of the ability to write musical notes (musical agraphia), tone deafness, etc., all of which are comprehended under the general term *amusia*. There is also a certain degree of independence both in the relation of these to one another and in their relations to aphasia. For example, a person may be able to sing and not to speak, or to speak and not to sing. It is probable that at least certain of the special clinical forms of amusia are anatomically independent, and that they are caused by lesions in the vicinity of those which produce the different forms of aphasia. The localization for that special form of amusia known as tone deafness, which is characterized by loss of the ability to recognize musical sounds as such, is probably in the first or first and second convolutions of the left temporal lobe in front of the region the destruction of which causes word deafness (Edgren).

§ 3. THE ASSOCIATION CENTERS OF FLECHSIG

The discussion in the preceding paragraphs has taught us that the higher functions of the brain which are in the immediate service of the mental faculties are carried out under the coöperation of several cortical regions. Brain anatomy has long since demonstrated various systems of fibers by which the two hemispheres and different regions of the same hemisphere are joined together. And quite recently our knowledge of the subject has been enriched so materially by the investigations of Flechsig that future researches in this field will have a much safer point of departure than hitherto.

A. ANATOMICAL

From what we have learned in preceding sections we know that only about one third of the entire surface of the cerebrum is in direct connection with tracts which mediate sensory impressions and arouse mental mechanisms. We know, moreover, both from the anatomical structure of the brain and from the fairly certain localization of cortical motor and sensory areas, that the remaining parts of the cerebral cortex have nothing whatever to do with afferent or efferent tracts. They serve to connect and associate the impulses delivered by the sensory nerves, to originate the resulting motor impulses, and to elaborate perceptions into higher mental processes; in short, these parts are to be regarded as the *organs of our purely psychical activities*. We shall speak of them in the following pages as the *association centers*.

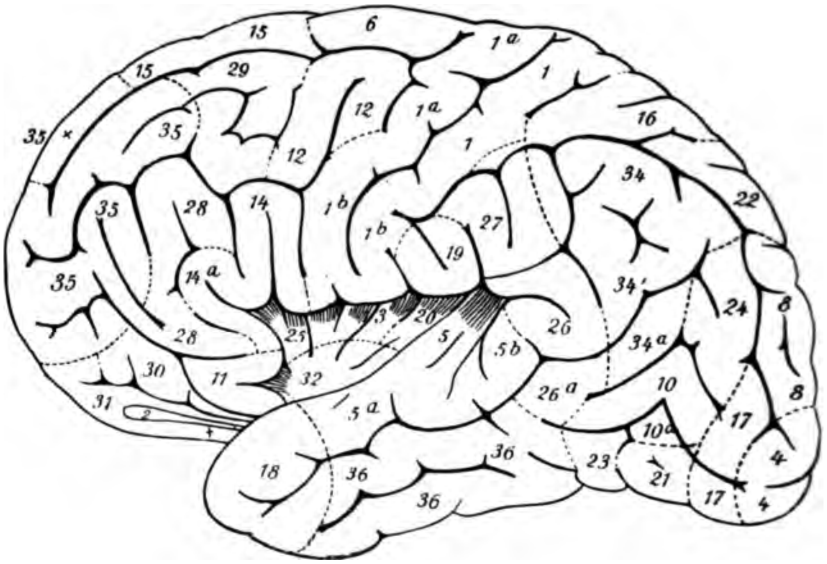

FIG. 297.—The myelogenetic areas of the human brain, outer surface, after Flechsig.

We find sufficient grounds for this view both in the clinical observations which have been made and in the results of anatomical investigation. The microscopical structure of these parts of the cortex alone indicates that they are of different character from the other cortical areas. While the cortical areas of the nerves of special sense possess in each case something which clearly recalls the distribution of nerves in the particular peripheral organ to which each corresponds, the association centers have more in common. Although they are scattered widely over the surface of the cerebrum, the microscopical structure is much the same type in all of them.

The same thing is taught by the mode of development of the myelin substance in the white matter of the brain. It is well known, through the work of Flechsig, that the fibers running to certain areas of the cortex receive their medullary sheaths much earlier than those running to other areas. In fact, at a time when the myelin substance in some convolutions is almost entirely complete, in others it is just beginning, and in still others has reached a medium stage of development. At certain stages, therefore, we can distinguish medullated, nonmedullated and half-medullated convolutions which present uniform structures throughout, and in all individuals of approximately the same age have practically the same relative position. Flechsig distinguishes thirty-six such "myelogenetic" areas. They are numbered according to the order in which they receive their myelin substance, and are divided chronologically into three groups.

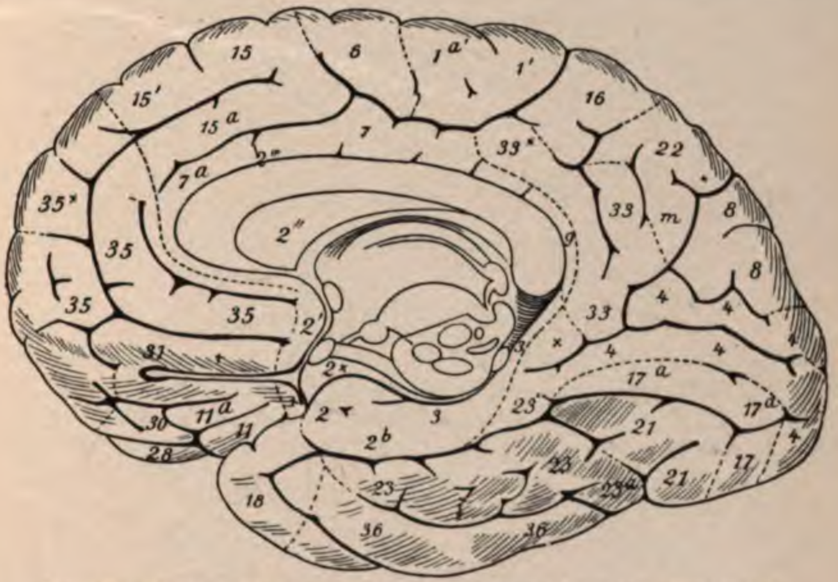

Fig. 298.—Myelogenetic areas of the human brain, inner surface, after Flechsig.

Those areas which are mostly myelinated at birth at term are called by Flechsig *primordial regions*: here belong Nos. 1 to 10, Figs. 297 and 298. Anatomically they are distinguished mainly by their great richness in paths to and from the subcortical centers (projection fibers). By comparison of Figs. 297 and 298 with Figs. 293 and 294, it may be seen that these areas embrace the points of entrance into the cortex of all sensory pathways as well as the points of exit of all the motor pathways. It is not known at present whether certain of these primordial regions (for example, No. 10, Fig. 297) are connected with peripheral end organs or not.

The second group of cortical areas includes the *intermediary regions* (Nos. 11 to 30) in which the myelination begins before the end of the first month after birth. To the third group, the *terminal regions*, belong those areas which are myelinated after the first month (31 to 36). In these as well as the most intermediary regions there are fewer projection fibers than in the primordial regions. Individual fibers indeed are to be demonstrated, but they are very scarce as compared with those in other tracts.

The terminal regions, on the other hand, are richest in association fibers, that is, in fibers running from one region of the cortex to the other; in fact they may be said to constitute the nodal points of the long association systems. But there are no long systems to be found which can be said to unite any two primordial regions regarded as sensory centers. A visual and an auditory impression, for example, could not meet in a primordial center: this could only happen in one of the intermediary or terminal regions.

The last named therefore constitute association centers. Three regions in each hemisphere are embraced by them, namely, a *frontal* or anterior, an *insular* or middle, and a *parieto-occipito-temporal* or posterior region. There is no reason to believe that these three are of equal importance for the psychical functions; in fact their positions with reference to the different sensory areas would seem to indicate that they have special functions. The posterior association center is intercalated between the visual, the auditory and the tactile areas; the anterior between the tactile and the olfactory—probably also the gustatory—areas; the middle between the auditory, the olfactory and the tactile areas.

The anterior center is formed by the anterior half of the first and the greater part of the second convolutions. On the basal side of the frontal lobe the gyrus rectus particularly belongs to this center. The middle center covers the insula. The posterior center embraces the precuneus, the parietal convolutions, parts of the lingual gyrus, the fusiform gyrus, the second and third temporal and the anterior portions of all three occipital convolutions (see Figs. 293 and 294).

B. THE ANTERIOR ASSOCIATION CENTER

We have already learned from observations on animals that extirpation of the frontal lobes produces noteworthy alterations in the intelligence and character of the animal. After removal of the most anterior portion of the brain, dogs become exceedingly irritable. Harmless, good-natured animals become fierce and malicious, so that after the operation they will not even allow themselves to be touched. The animal's movements are exceedingly cumbrous and awkward. He cannot hold a bone firmly, his whole carriage of himself is unsteady, he stumbles easily and on a slippery floor at once loses his footing (Goltz).

In line with this, Bianchi has observed that the intelligence with which a monkey performs complicated acts is often greatly affected by the removal of both frontal lobes.

Similar changes in character have not infrequently been observed in men with lesions of the frontal convolutions. Persons, who before were well disposed and orderly, became foolish, impatient and headstrong, and at the same time changeable and fickle. Neither sensory nor motor disorders of any kind can be demonstrated on them (Welt).

Flechsig has given the following description of the effects of lesions in the frontal association centers observed on men. The patient sometimes loses all sense of his actual relations to the world, imagining himself possessed of great wealth, or the recipient of high honors; sometimes he confuses perceptions of external objects with the inner consciousness of his own person, or *vice versa,* his consciousness of himself with impressions of the outer world, so that he either forgets that he exists or takes no notice of his surroundings. There need be no confusion of ideas in the strict sense of the term. He may speak rationally and in a perfectly orderly way about various subjects within his mental grasp, but he is unable to distinguish between the true and the false, the imaginary and the real, the possible and the impossible; and along with this defect of the logical sense there goes a loss of the ethical and esthetic judgments, so that he does things which are utterly irreconcilable with his former character. The patient thus loses his composure, and this to a greater degree the more he is actuated by strong feeling or is under the influence of passion. When once he becomes angered, a fit of rage comes over him like an avalanche. A stage is finally reached where all self-control is lost and he is ruled in everything merely by the logic of madness. Whatever is uppermost in his mind he does without regard to his surroundings or to good taste. At last imbecility sets in and the personality is lost entirely.

C. THE POSTERIOR ASSOCIATION CENTER

Goltz observed the following effects of removing the occipital lobes from dogs. The tactile sense was undisturbed, the animal was not merely able to move all the muscles of his body voluntarily, but could perform all kinds of movements with almost as much facility as a normal animal. He had no trouble in eating and could hold a bone between the paws, etc.

If the animal were vicious before the operation, removal of the occipital lobes made him docile. Nothing then served to excite him; he was always calm and deliberate. But his perceptive faculties suffered considerable diminution and his intelligence sank to a low level.

In man lesions within the posterior association center have been observed to produce alexia (cf. page 663), and a more or less distinctive loss of the power to interpret visual impressions of other kinds. All such disorders, whatever their extent, are included under the term "mind blindness" given by H. Munk.

Typical mind blindness in man is characterized by v. Monakow in the following manner: The person affected has impressions and sensations of light but can no longer recognize the objects of his surroundings. This is not because his memory pictures of the objects are gone, but because the associations necessary for understanding them are no longer possible, that is, the memory pictures cannot be called up by the retinal stimulus, although they may be aroused by another sense, or quite spontaneously. Among other things a person can tell one color from another but cannot find the right names for the colors. He cannot tell just the quality of the color of the sky, or of leaves, or of blood, etc.

While the memory for many different forms of visual impressions may be just as good as ever, it appears as a rule to be considerably impaired for recent impressions. Such patients are unable to describe the forms of objects presented to them just a moment before, while they have a perfectly clear picture of objects with which they are familiar, such as a knife or a watch, and can describe them. They can also acquire new optical images, but it is much more difficult than formerly. Sometimes the memory for old and familiar objects as well as for less familiar ones is affected and the person cannot describe well-known buildings and streets of his own town so as to direct another person how to go from one point to another. In severe forms of mind blindness all objects and persons alike appear strange, and may not be recognized even in their general relations.

What the patient is unable to recognize by optical impressions alone, he can, however, properly orient by means of other impressions—for example, auditory impressions. Thus a patient who fails to recognize his own friends by sight may recognize them by their voices, etc.

Mind blindness comes on if the lesion extends to the white matter of the occipital lobe, and in all probability is caused by the interruption of the association pathways and by injury to the association areas. It is not referable to any definite locality, but can be produced by abscesses in different parts of the lobe. In the great majority of cases thus far observed, the abscesses are situated in both hemispheres. Mind blindness has not yet been observed as the result of disease on the right side alone.

The phenomena of mind blindness undoubtedly show that the occipital lobes play a determining part in the proper evaluation of optical impressions. Observations on more extensive lesions of the posterior association center, in Flechsig's sense, teach us also that mental disorders of a more serious nature may result from the loss of its function.

The first symptom of a diseased condition involving a large part of this center is incoherence of ideas, that is, a primary intellectual deficiency and something quite independent of the effects which follow purely and simply as the result of a loss of ordinary associative connection of external impressions. Many of these patients exhibit no lack of clearness as to their own person, evince no lack of composure in their conduct, no deep perversion of their feelings or desires; but they do not correctly interpret external objects, and consequently misuse them. They mistake one person for another, and lose their bearings both spatially and temporally. The mental images of what goes on outside are lost, consequently a clear understanding of the external world and that knowledge of it which is capable of being put into words; in short, all empirical interpretations of external impressions are reduced to naught. The patient has thus become impoverished for ideas, eventually nothing either true or false enters his head—he has become an idiot.

D. FINAL SURVEY

It is likely that in the more complicated mental processes all the association and sensory centers coöperate, since they are united with each other by numerous nerve fibers, and that from this coöperation results the harmony of the cerebral functions.

Flechsig has worked out some views with regard to the mechanics of the higher brain functions, which I shall abstract briefly here, because among modern researches on the brain which have a physiological bearing those of Flechsig undoubtedly take first rank.

Since the *memory* always suffers to a great extent from destruction of the association centers, the nervous elements with which the ability to recall sense impressions is connected must unquestionably be sought mainly in those centers. The ganglion cells play the chief rôle in this because, so far as our experience yet goes, they alone of all the nervous elements are able to store up impulses and to become charged with energy. Without knowing anything about it, we may suppose that the number of nerve elements which are active in the simplest event of consciousness must be very great.

What we do know with certainty is, that tokens of memory (memory pictures) which are imprinted, so to speak, in the brain elements are more or less firmly related to each other; and the basis of this organic unity of memory lies in the systematic arrangement of the numberless disparate constituents of its physical groundwork.

The question as to what are the physical forces which bring the memory pictures back to consciousness is one of particular interest. We commonly attribute the greatest importance to our sense impressions, impressions of the outer world, and, as a matter of fact, throughout our waking hours, these are all the time rousing memory tokens.

But a second important factor comes in here. External impressions act to rouse the imagination or a reflective train of thought most potently if they at the same time rouse certain feelings or emotional impulses. Anything that pleases not only stimulates but also quickens the imagination. But hunger, thirst, sexual passion and many other bodily sensations have a direct summoning influence on all agreeable ideas connected with them. We have then in the bodily feelings and general bodily spirits, which are the real primary forces of the imagination, a second regulating factor upon which rests a very substantial and by no means the most sordid part of art and poetry.

Primarily the senses appear to be only subordinate helps to the impulses coming from within, but they provide us a store of material for the expression of our feelings. The artistic perfection of the pictures which we create with our minds will depend in large part upon the care with which this preparatory work is done, upon the sharpness of our grasp of the actual; and the imagination will work to a given end the more effectively, the more this sensory material is allowed to appeal to our feelings, and so to take on tokens by which it can be recalled to mind.

But even in the most magnificent creations of the imagination we have to do to a certain extent with simple mechanical processes. Here again conducting pathways, nerve fibers, which connect the mechanisms concerned in the production of bodily feelings with the central workshops of organized memory, namely the association centers, have a part to play. And since the nerves which serve to bring the sensory impulses to consciousness push through to the cortex and enter the sensory centers, we have converging toward the same cortical regions nerve paths which make us aware of the treasures and charms of the outer world, and those which bring to consciousness the everyday needs of the body in the form of desires. Both without distinction act from these their highest points of attack upon the motor mechanisms on the one hand and upon the intellectual centers on the other.

The pathways between the centers which rouse our desires and the intellectual regions of the cortex are not called upon merely to clothe the content of sense experiences in ideas, to idealize them in short, nor merely to facilitate their satisfaction by recognition of means to that end. But there is set up along some associative pathway an interplay, a working of ideas which leads to the maturation of *self-consciousness* as a contest between sense and reason. Along with inciting impulses there arise some with which feelings of restraint are connected—and thus the discharge of memory pictures through the bodily desires comes to have a distinctly moral significance. The motives are necessarily robbed of all their ideal character—the struggle between the sensuous and the moral feelings is sure to lapse, the moment the force of the intellectual centers is paralyzed and the rational content of the emotions disappears. Control of the emotions requires a powerful cerebrum, which probably means in the first instance soundness of the frontal association centers.

A purely mechanical factor is concerned in this control of the lower impulses of the cerebrum. In so far as the bodily impulses do not arise by the automatic excitations of the central nerve cells, they belong by nature to the category of reflex processes, and like all reflexes are continually held in check by the cerebrum. When the cerebrum becomes weak this mechanical restraint is relaxed and the bodily incentive gains greater control over the rational centers.

Through the investigation of the material conditions of the mind's activity, medicine is thus brought into immediate relations with the moral sciences, and it is indeed conceivable that once she has properly grasped the problem, she will unhesitatingly press forward to the front rank of those forces which have made the moral elevation of mankind their chief concern. Investigation to-day is not led, as was the philosophy of the Enlightenment in the Eighteenth Century, by an instinctive hatred for the dogma of the immateriality of the soul, for that dogma in no way prevents our undertaking the moral elevation of the race from the bodily side. What we must insist upon is merely this—that the moral powers of the mind like its other powers depend to a great extent upon the body.

A general clearing up of problems pertaining to the hygiene of the brain is therefore eminently necessary. Much remains to be done along this line, if we are to succeed in strengthening and establishing the natural grounds of the moral feelings even for future generations. Certain it is that our efforts will be successful in a measure directly proportional to the opportunities afforded the mentally and morally unfortunate of profiting by the deeper insight and better desires of those whose lives are ruled by high ideals.

But it is not alone the practical goals of life of which we get a glimpse in these considerations of the mechanics of the mind. As that which we already realize to be one of the noblest sides of our being, and which is bestowed on mankind in virtue of the intellectual centers of the brain, becomes embodied in the desire to comprehend the natural order of things in the realm of spirit also, the real advances of our knowledge in this realm of natural science lead us with the compelling force of a natural law at last to an ideal view of the world. The more the true magnitude of the real power resident in the realm of mind itself is revealed to us, the more clearly do we feel that back of the world of phenomena powers are at work for which human knowledge can scarcely find an adequate metaphor.

§ 4. THE TIME CONSUMED BY PSYCHOPHYSICAL PROCESSES

There remains for us to summarize briefly what has been discovered with reference to the time occupied by psychophysical processes.

The point of departure in all investigations of this subject is the time required for a person to react with a definite voluntary movement to some external stimulus (*simple reaction time*). It will be apparent at once that some measurable time is required for such reactions, if we but reflect that the propagation alone of a stimulus along the afferent and efferent nerves concerned consumes a certain amount of time (cf. page 417). But in the process which we are considering now, something takes place in the sensorium and something in the motor region, and between these something, probably, elsewhere in the cortex, all of which constitute the psychophysical factors. The special interest attaching to these determinations is that they will give us some information as to how much time is required for these purely central processes.

Experiments in this field are usually carried out by having the subject of the experiment open the current of an electric signal the moment he receives a given stimulus. If, for example, the reaction time is being taken for an auditory stimulus, it is necessary to have in the same electrical connection: (1) the signal, (2) a key for the subject, (3) a key by which the current is closed by the director of the experiment and which at the same instant causes a sound to be made by (4) an electric bell or other device. The sound which is made when the current is closed constitutes the stimulus to which the subject reacts by opening the current. If the electric signal be arranged so as to record on a moving surface the instants of opening and closing, the time which intervenes will be the reaction time. This time can be determined directly if a clockwork whose hands mark thousandths of a second be set in motion by the closing and stopped by the opening of the current. Such an instrument is known as a *chronoscope*.

The simple reaction time varies all the way from 0.11 to 0.55 second according to the nervous organization of the subject, and the kind of sensory stimulus employed. Likewise if a series of experiments be carried out on the same person and with the same kind of stimulus, only varying in strength, a considerable variation in the reaction time is noted, which cannot be due to any variation in the rate of propagation in the nerves exercised, consequently must be accounted for by differences in the time consumed in the psychophysical processes. Such variations moreover can be perceived subjectively, so that one can tell within 0.05–0.06 of a second whether a given reaction time was longer or shorter than a previous one. Remembering that the propagation of the sensory stimulus before it rouses the conscious sensation, as well as the motor impulse after it has once been discharged, is an entirely unconscious process, we see that the time subjectively estimated covers the span between perception of the sensory impulse and release of the voluntary impulse.

The following table will give us some idea of the reaction time for the different senses:

AUTHOR.	Sight.	Hearing.	Electric stimulation of the skin.
Hirsch	0.200	0.149	0.182
Hankel	0.206	0.151	0.155
Donders...............	0.188	0.180	0.154
v. Wittich.	0.186	0.182	0.130
Wundt.................	0.222	0.167	0.201
v. Kries	0.193	0.120	0.117
Auerbach	0.191	0.122	0.146
Buccola	0.168	0.115	0.141

For the sense of taste v. Vintschgau has found the following reaction times for common salt, sugar and quinin: tip of the tongue, 0.597, 0.752 and 0.993 second respectively; for the base of the tongue, 0.543, 0.552 and 0.502 second respectively. The reaction time for different odors (oil of peppermint, oil of rose and bergamot oil) varies in Moldenhauer's findings between 0.199 and 0.374 second.

It is not surprising that the reaction times found by the different authors for a given sense differ considerably, for the nervous organization of the subject has always to be taken into account.

In most cases it requires some time for odoriferous and sapient substances to come in contact with the appropriate nerve endings; hence the longer time consumed by a reaction to these stimuli than to others.

The differences observed between the reaction times for sight, hearing and touch are, as Wundt remarks, probably dependent upon the different intensities of these stimuli. For one and the same sense the reaction time is always shorter the stronger the stimulus. We cannot ordinarily compare the intensity of a certain auditory stimulus with that of a certain visual stimulus, for there is no standard of measurement common to the two. The threshold stimuli for the different senses, however, being in all cases just sufficient to produce an effect, must be relatively of the same strength. Wundt found in fact that the reaction times for the visual, auditory and tactile stimuli in the neighborhood of their threshold values were almost exactly equal, namely 0.331, 0.337, and 0.327 second respectively. We infer from this and the facts summarized in the table that auditory stimuli in general are more powerful than optical or cutaneous stimuli.

The reaction time is increased as the body or mind becomes fatigued, also as the result of all sorts of exciting influences, but is reduced by practice, in some cases very considerably. All this goes to prove that the length of the reaction time depends essentially on the duration of the psychophysical process, or in other words, that we dare not look upon the psychophysical process as a perfectly constant factor.

If warning be given of the signal just before it is made, the reaction time is considerably shorter than otherwise. The subject has his whole attention fixed on the coming event, and, by sufficient practice, he can make the central connection so tense as to give the response almost as promptly as if it were a pure reflex. The muscular process particularly is facilitated in this way and the reaction is then described as *muscular reaction*. A reaction in which the attention is strained more especially to receive the impression is called a *sensory reaction*. If the attention be not first aroused, it requires more time also to perceive a stimulus. Thus Wundt found in one experiment with the auditory stimulus that when warning was given the sound was heard in 0.076 second, when not given, in 0.253 second.

The study of the changes produced in the reaction time by nerve poisons, such as alcohol, coffee and tea, is an important means of learning the physiological effects of these substances.

If instead of a single stimulus, a series of stimuli following each other at a definite interval be given, the reacting person repeats the rhythm to a certain extent independently, and the reaction time sinks to nil. An absolute determination of the time cannot be made under these circumstances: the reaction may take place either at the instant of stimulation, or a little after or even a little before. According to Martius the errors amount to ± 0.01 of a second.

We very often meet with phenomena of this kind in our everyday life. The playing of an orchestra under the direction of a leader, dancing and marching to music, are all cases in point; likewise the enumeration of heart beats. But if the rhythm of stimuli be not perfectly uniform and the intervals not exactly equal, it is impossible to react to them synchronously, and the ordinary reaction time comes into play again. By varying the method of experimentation, we can penetrate still farther into this question of the time consumed by the psychophysical process. The methods employed for this purpose can best be explained by a few concrete examples.

Suppose the stimulus be applied either to the right or left foot: in the first case the subject is to respond with the right hand, in the second with the left. He has then not only to perceive a stimulus, but to distinguish a definite property and to choose between two movements. On the average the time required for this reaction is, according to de Jeager, 0.066 second longer than the simple reaction time.

In the case just given the choice was a relatively easy one, because a stimulus on one foot naturally suggests a reaction with the hand of the same side. But if the experiment be so arranged that when a red disk appears the subject is to react with the right hand, and when a blue, with the left, the time is on the average 0.154 second longer than the simple reaction time. The psychophysical processes in this case are of exactly the same kind as the former: the greater interval of time is due to the fact that there is no natural connection between the sense impression and the movement, consequently the choice is more difficult. The time is shorter if a reaction be required for only one of two stimuli. For example, a red or a blue disk may appear: the subject is to react to the latter, but not to the former. The time is then on the average 0.034 second longer than the simple reaction time and thus 0.12 second shorter than in the case last mentioned. The principle of this method of simple choice is exactly the same as the other: the individual must recognize a definite quality in the stimulus and choose between acting and not acting. But the reason why the choice can be made more quickly is that the attention is concentrated on the particular impression which calls for the reaction. The time found is practically the time required to perceive a given quality in an impression, and is called the *discrimination time.*

APPENDIX

NOURISHMENT OF THE BRAIN

1. *Blood Supply.*—As already remarked at page 572, the normal activity of the brain is very much dependent on the blood supply. If the blood supply is greatly diminished, unconsciousness is the result; this usually happens, for example, when the carotids are compressed. Convulsions may also be produced in the same way. Thus if the right innominate artery and the left subclavian central to the vertebral be ligated in a rabbit, the animal almost immediately falls into convulsions.

Variations in the blood supply to the brain have been discussed at page 240.

In cases of accidental defect in the skull, the brain pulsates in grown persons just as do the fontanels in young children. Mosso has found on such persons that the blood supply to the brain increases with mental work, and to a marked degree also when the person is under strong emotional excitement, and that the vessels to the extremities become at the same time constricted.

If now it is true, as supposed by the majority of authors, that vasomotor nerves are wanting in the vessels of the brain, such changes in the blood supply can only be explained by supposing that in mental work or under the stress of emotions the vasomotor center is stimulated and constriction produced in various extracranial vascular regions.

Likewise in undisturbed sleep, when no conscious processes are going on in the brain, the blood supply to the brain may be increased by all sorts of sensory stimuli, without waking the individual.

2. *Fatigue and Sleep.*—Not only mental work but the waking condition of itself fatigues the brain, or more correctly the cerebrum, and it must from time to time be given an opportunity to recuperate. This recuperation of the brain takes place in sleep. If a person is denied sleep for a long time, very profound physical and mental disorders result.

Experiments have been made to determine the soundness of sleep by finding the threshold value of an auditory stimulus necessary to wake the person at different intervals after he fell asleep. According to Mönninghoff and Piesbergen, the depth of sleep increases very gradually up to the second quarter of the second hour. Within the second and third quarters of the same hour it increases very rapidly and very greatly and then decreases just as rapidly up to the first quarter of the third hour. From this point onward there is a gradual decrease of depth which continues to the second half of the fifth hour. Here a second slight rise begins, but the level is comparatively uniform from about the fifth hour onward (cf. Fig. 299).

Metabolism is less active in sleep than in the waking condition and the falling off is greater the sounder the sleep. If the carbon dioxide output be taken as a measure of the metabolism, that of sleep is related to that of the waking condition (not working nor yet completely resting) as 100:145. This reduction of metabolism in sleep is dependent in the main upon the cessation of voluntary movements, for it may reach just as low a level in the waking condition if the muscles be completely relaxed and every voluntary motion be suppressed (Johansson).

According to some experimental determinations the carbon dioxide elimination reaches its minimum in the second hour of sleep, and this probably constitutes to a certain extent the expression of the deepest sleep in a sleeping period of perhaps six to eight hours.

The following peculiarities have also been observed in sleep. The eyes with pupils contracted are turned inward and somewhat upward. The respiratory movements are less frequent than in the waking condition, and even in the man are mainly of the costal type. The respirations are also sometimes periodically suspended. The heart action is retarded; the vascular tone decreases in the cutaneous vessels and probably also in the visceral vessels, and as a consequence the blood pressure falls. This in its turn is said by many authors to cut down the supply of blood to the brain, to produce in short a condition of cerebral anæmia.

Howell has observed the volumetric variations of the hand and the lower part of the forearm in sleep by means of the plethysmograph, and has found that the amount of blood in the part increases gradually from the beginning of sleep and reaches its maximum within one to one and three-quarter hours. It remains at this level until about three-quarters of an hour before awakening and then falls rather rapidly to the end of sleep.

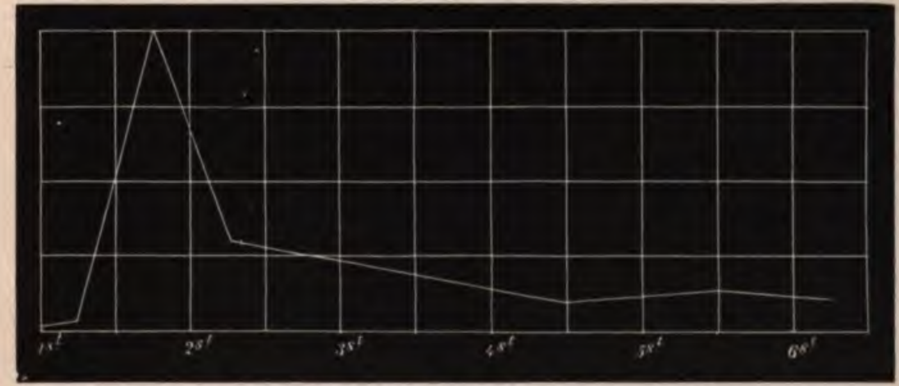

FIG. 299.—Curve representing the depth of sleep, after Piesbergen. The abscissæ represent hours.

The inception of sleep is favored by cutting off the sensory stimuli, especially if the attention be not kept aroused by any active mental processes. Strümpell has reported a case in which the patient became blind in one eye and deaf in one ear merely by stopping all cutaneous sensations. As soon as the good eye was closed and the functional ear was stopped he fell asleep.

Sleep does not depend entirely upon processes going on in the cerebral cortex, for as mentioned at page 623 a change from the sleeping to the waking condition and vice versa can be observed on decerebrated animals.

[Perhaps the most satisfactory theory which has yet been given to explain the cause of sleep, is that of Howell. The dilatation of the cutaneous vessels during sleep observed by this author, taken in conjunction with many other observations that there is during sleep a reduction of the general blood pressure, and that there is at the same time a diminished blood flow to the brain, suggested the idea that the depression of the psychical activities below the threshold of consciousness is due primarily to anæmia of the brain (cf. page 240). To account for this anæmia Howell supposes that that portion of the vasomotor center which maintains the tonus of the cutaneous vessels periodically becomes fatigued, just as the cells of the cortex which mediate the psychical processes may be supposed also to become fatigued. If under these circumstances the usual external stimuli which serve to keep the vasomotor center active be withdrawn; as for example, the eyes be closed, noises be excluded and the voluntary muscles be relaxed, the vasomotor center relaxes its control of the cutaneous vessels, the resulting dilatation withdraws blood from the cortical cells and the consequence of this is a further and a comparatively sudden decline of cerebral activity below the threshold of consciousness. When the vasomotor center has been recuperated it reasserts its activity, blood is again supplied to the cortical cells and consciousness returns.—Ed.]

3. *The Temperature of the Brain.*—By means of a very delicate thermometer Mosso made a careful study of the temperature of the brain in animals and in men with defects in the cranium, and found among other things that on account of its slight covering it has a lower temperature than the rectum. But a rise in temperature is caused by the local effects of atropine, cocaine and alcohol, by electrical stimulation, by anæmia and asphyxia—in all these cases due to alterations in the circulation. Chloroform, painful sensations, etc., produce no change in the temperature of the brain worth mentioning. In like manner the conscious activities of the brain produce so slight an effect on the temperature that they cannot be recognized, or else they occur along with other processes, as the result of which the brain is cooled, even though the psychical functions continue.

On the other hand some unconscious processes brought on by external agencies increase the temperature of the brain.

4. *The Intracranial Pressure.*—The cerebro-spinal fluid filling the subarachnoid space exerts a pressure on the walls of the cerebro-spinal canal, which when measured by a manometer of suitable construction inserted into an opening in the skull, is found to be about equal to the venous pressure (5–10 mm. of Hg.), if the animal is in a horizontal position. When the hind parts of the body are raised above the head the pressure becomes greater, when they are lowered it falls and may even become negative (Sivén).

According to Bayliss and Hill, there is no mechanism for maintaining a constant intracranial pressure; the functions of the brain appear, within wide limits, to be independent of intracranial pressure, so long as the circulation is not impaired. If the foramen magnum be constricted so as to obstruct the circulation, the centers of the medulla may be affected and, among other things, the respiration be retarded and finally stopped, the heart action retarded, and the blood pressure increased.

The outlet for the cerebro-spinal fluid is by way of the veins. Within fifteen to thirty minutes after injection of methylene blue, in a salt solution into the cranial cavity, the color appears in the urine (Hill).

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CHAPTER XXV

PHYSIOLOGY OF SPECIAL NERVES

The innervation of the different organs and organ systems has been discussed in connection with their functions, hence in this chapter we need only present the physiology of special nerves in the broadest outlines. For details and controverted points, reference must be made to the previous chapters of this book, and for the purely anatomical data to the text-books of anatomy.

§ 1. THE CRANIAL NERVES

I. The *olfactory*, or the nerve of smell (cf. page 486).

II. The *optic*, or the nerve of vision (cf. page 508), contains not only afferent but efferent fibers.

III. The *oculomotor*, or the common nerve of the eye muscles, innervates the levator palpebræ superioris, the superior, inferior and internal recti, the inferior oblique, the ciliary muscle or the muscle of accommodation (cf. page 532) and the sphincter of the pupil (cf. page 528).

IV. The *trochlearis*, or *patheticus*, innervates only the superior oblique muscle of the eye.

V. The *trigeminal*, or *trifacial*, contains both afferent and efferent fibers.

The efferent fibers innervate the jaw muscles (masseter, temporal, pterygoids), also the mylohyoid, the tensor palati and the tensor tympani (cf. page 497) and the anterior belly of the inferior digastric. Besides it is stated that the trigeminal contains secretory fibers for the lachrymal glands and the sweat glands of the face, vasodilator fibers for the skin of the face and the eye, etc.

The afferent fibers of the trigeminal constitute first, the sensory nerves of almost all the skin of the face, of the eye, the nose, the mucous membrane of the mouth, the tongue and the teeth. Secondly, the trigeminal carries a number of nerves of taste (cf. page 484).

VI. The *abducens* innervates the external rectus and is said also to contain fibers for the sphincter of the pupil.

VII. The *facial*, or nerve of expression, contains secretory fibers for the submaxillary, sublingual (cf. page 257) and lachrymal glands, vasodilator fibers for the submaxillary glands and anterior part of the tongue, and motor nerves for the stapedius muscle. Its chief significance, however, is that it innervates the muscles of the face by contraction of which the skin of the face is folded in various ways, producing the different expressions.

VIII. The *auditory*, or nerve of hearing, by its cochlear root mediates auditory sensations (cf. Fig. 199) and by the vestibular root (cf. page 473) the various functions of the semicircular canals and otolith sacs.

Various experimental observations indicate that the vestibular root probably has no significance whatever for the auditory sensations. Since the eighth cranial nerve therefore is at least not exclusively auditory in function, J. R. Ewald has proposed that it be simply called the eighth nerve (N. octavus).

IX. The *glossopharyngeal* conveys, besides some motor fibers to the tongue and pharynx, secretory fibers to the parotid glands (cf. page 257) and vasodilator fibers to the anterior pillars of the fauces and tonsils. Among its afferent fibers are the taste fibers, also sensory fibers for the mucous membrane of the tympanic cavity and Eustachian tube.

X. The *vagus*, or *pneumogastric*, and

XI. The *spinal accessory*.

In view of the fact that these two nerves are intimately related anatomically and that diverse views are held as to the share each takes in controlling the organs innervated by them, it is most profitable to consider them, as Grossman has proposed, as one nerve composed of three bundles named, in order of their exit from the medulla, the upper, middle and lower. The upper bundle can readily be separated in the monkey and in man from the glossopharyngeal. The lower bundle is the outer branch of the spinal accessory which innervates the trapezius and the sterno-cleido-mastoid muscles. There remains then the trunk composed of the vagus and the inner or true accessory branch in which are to be distinguished an anterior and a middle portion.

According to the experimental results of Kreidl on the monkey, motor nerves pass in this anterior portion (the vagus of anatomists) to the palatoglossal and palatopharyngeal muscles as well as to the constrictors of the pharynx and œsophagus. Moreover, it is here that the motor fibers of the superior laryngeal are found, also the afferent pulmonary fibers which assist in the automatic regulation of respiration, and in the rabbit, dog and cat at least, the depressor fibers (Fuchs, Codman; cf. page 193).

In the middle bundle (accessory of the anatomists) are the inhibitory fibers of the heart (cf. page 188), the motor fibers for the levator palati and the motor fibers contained in the inferior laryngeal nerve.

In the trunk of the vagus are the following fibers, the origin of which is not fully known: (1) efferent fibers. *a.* To the circulatory organs: accelerator fibers to the heart (page 191); vasoconstrictor fibers for the heart, the stomach, intestine, kidneys, spleen, and possibly the lungs (page 240); vasodilator fibers for the coronary vessels and the lungs (page 235). *b.* Digestive organs: motor nerves for the stomach (page 284), the small intestine and the upper part of the large intestine (page 289); inhibitory fibers for the cardiac sphincter of the stomach and the longitudinal muscles of the small intestine (pages 284, 289); secretory nerves for the gastric mucosa and the pancreas (pages 263, 269). *c.* Respiratory organs: motor and possibly inhibitory fibers for the bronchial muscles (page 324).

(2) Afferent fibers. Respiratory organs: afferent fibers from the larynx (page 330).

XII. The *hypoglossal* innervates the musculature of the tongue.

§ 2. SPINAL NERVES

The anterior and posterior roots of the same side belonging to each segment of the spinal cord unite peripherally to the spinal ganglion to form a mixed nerve trunk. Each of these nerve trunks then divides into a dorsal and a ventral branch. The dorsal branches are relatively small and supply only the skin and muscles of the back; the ventral branches, which are much larger, are allotted to the anterior and lateral parts of the neck, thorax, abdomen and extremities.

The dorsal branches all run separately to their destination; but with the exception of the twelve thoracic nerves, the ventral branches anastomose freely with one another, forming plexuses corresponding to the main divisions of the body.

A number of experimental and clinical researches have been made on the distribution of the fibers arising from the different roots. We shall here pay regard chiefly to the exposition given by Kocher on the relations obtaining in man.

A. SENSORY NERVES

Each spinal nerve root, even if its fibers unite with others to form a plexus, supplies a continuous region of the skin. These regions overlap, however, so that a single region on the lateral aspect of the body is provided with a twofold or even a threefold supply (Sherrington).

Fig. 300 represents schematically, according to Kocher, areas of distribution of the different spinal roots. This is constructed on the basis of clinical observations of patients with total lesions of the spinal cord. The boundary lines in the figure mark the upper limits of sensibility for lesions at the different levels. In reality the regions supplied by the different nerves, in man as in animals, overlap considerably both above and below. The areas blocked out in the figure represent therefore the *central parts* of the fields actually supplied by the separate roots.

B. MOTOR NERVES

In the following table are summarized, after Kocher, the distributions of the different *motor roots*:

ROOT.	MUSCLES.
I C.	Small neck muscles; sternohyoid; sternothyroid; omohyoid.
II C.	Sterno-cleido-mastoid; trapezius.
III C.	Platisma myoides.
IV C.	Scaleni; diaphragm.
V C.	Rhomboidei; supra- and infraspinatus; coracobrachialis; biceps; brachialis anticus; deltoid; supinator longus and brevis.
VI C.	Subscapularis; pectoralis major and minor; pronator teres and quadratus; latissimus dorsi; teres major; triceps; serratus magnus.
VII C.	Extensors and flexors of the wrist.
VIII C.	Extensors and flexor longus of the fingers.

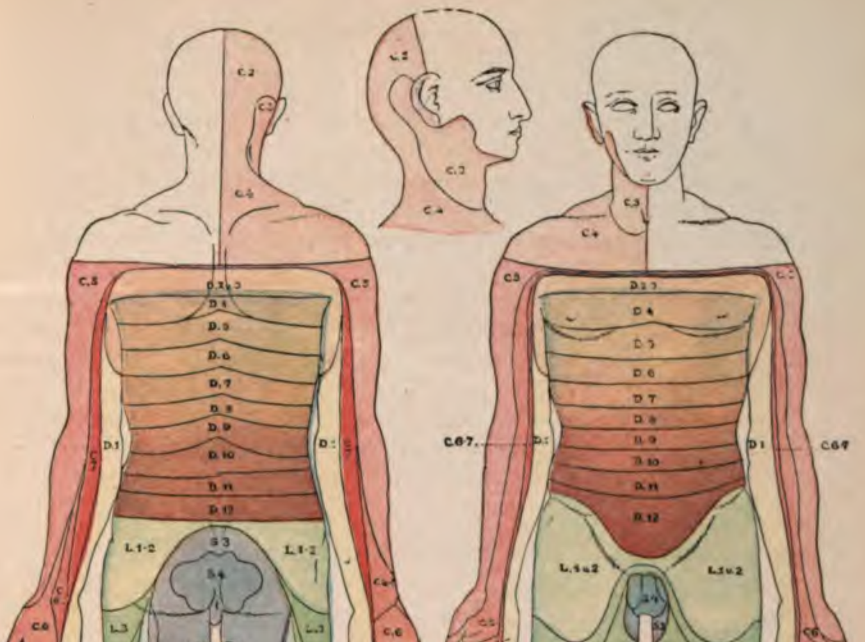

Fig. 2. *Fig. 1.*

FIG. 300.—Distribution of the superficial areas served by the different sensory roots, after Kocher.

Red: area of cervical roots—C_2 to C_7.
Yellow: area of dorsal roots—D_1 to D_{12}.
Green: area of lumbar roots—L_1 to L_4.
Blue: area of sacral roots—S_1 to S_4.

I T.	All the small muscles of the hand and fingers.
I–XII T.	Muscles of the back.
I–XI T.	Intercostal muscles.
VII–XII T.	Abdominal muscles.
I L.	Lowermost parts of the abdominal muscles; quadratus lumborum.
II L.	Cremaster.
III L.	Psoas; sartorius; iliacus minor; pectineus; adductors of the thigh.
IV L.	Quadriceps femoris; gracilis; obturator externus (?).
V L.	Gluteus medius and minimus; tensor fasciæ femoris; semitendinosus; semimembranosus; biceps.
I S.	Pyriformis; obturator internus; gemelli; quadratus femoris; gluteus maximus; long extensors of the foot and toes; peroneus longus and brevis.
II S.	Long flexors of the foot and toes; large calf muscles; small foot muscles.
III S.	Ejaculator muscles; muscles of the perineum.
IV S.	Sphincter and detrusor muscles of the bladder; sphincter ani.
V S.	Levator ani.

The same must be said of this summary that was said of the sensory nerves, namely, that a given muscle is supplied by more than one spinal root. Accordingly the data given here indicate the central regions of distribution, or, the other way about, the *chief nerve supply* for the separate muscles. Starr finds, for example, that the scaleni muscles are innervated by the second and third cervical roots, the diaphragm by the third and fourth, the deltoid by the fourth and fifth, the biceps by the fifth and sixth cervical, the sartorius by the first and second lumbar, the quadriceps femoris by the second and third, the adductors of the thigh by the third and fourth, etc.

It was formerly asserted by Preyer and Krause that the skin covering any given muscle is supplied with sensory fibers by the same spinal nerve as that which supplies the underlying muscle with motor fibers. Sherrington finds, however, that this is not the case; for certain displacements occur causing the skin region to be situated farther distally than the corresponding muscle. The flexor sides of the thigh and fore leg and the extensor side of the arm appear to be the only exceptions to this rule. The different sensory fibers of the muscles themselves appear to belong to the same segment as the motor fibers.

§ 3. THE SYMPATHETIC NERVES

A. RELATIONS OF THE SYMPATHETIC NERVES TO THE CENTRAL NERVOUS SYSTEM

The nerve fibers traversing the sympathetic nerves are both afferent and efferent in function; and they mediate a great variety of functions not under direct influence of the will. To these belong the vasoconstrictor and vasodilator nerves, accelerator nerves of the heart, motor and inhibitory nerves of the stomach, intestine, bladder, etc. They constitute therefore the greater part of the visceral nerves. It is justifiable to enumerate along with the components just named the visceral fibers contained in certain cranial nerves and those arising from the sacral roots. Doing this, we can then say, that the *sympathetic* or *autonomic* (Langley) *nervous system* presides over all of the functions not under the direct control of the will.

All these nerves agree in having their origin in the central nervous system. In the strict sense the sympathetic nerves constitute processes of the lateral horn cells on the same side of the cord.

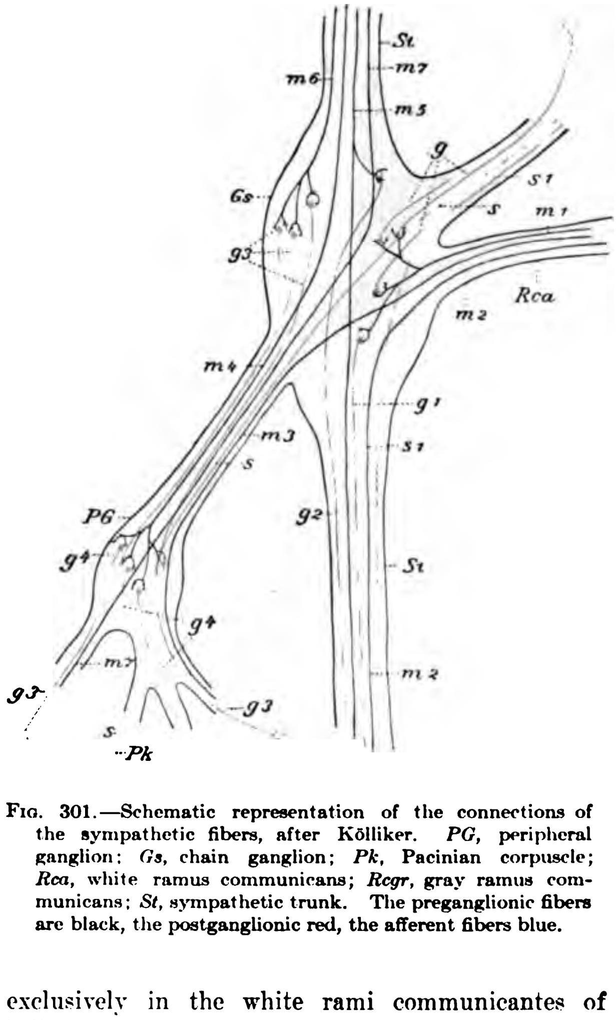

FIG. 301.—Schematic representation of the connections of the sympathetic fibers, after Kölliker. *PG*, peripheral ganglion; *Gs*, chain ganglion; *Pk*, Pacinian corpuscle; *Rca*, white ramus communicans; *Rcgr*, gray ramus communicans; *St*, sympathetic trunk. The preganglionic fibers are black, the postganglionic red, the afferent fibers blue.

The efferent fibers belonging to the autonomic nerves are slender in comparison with other efferent nerve fibers, and, unlike the motor nerves to the skeletal muscles, connect somewhere along their course with ganglion cells from which new fibers issue to complete the pathway.

The afferent fibers found in the sympathetic nerves are for the most part offshoots from the ganglion cells in the spinal ganglia; there are among them some which spring from peripheral ganglion cells, and thus constitute true sympathetic fibers.

The most important visceral fibers of the cranial nerves have already been studied. We have then to consider only the visceral fibers coming from the spinal cord.

The *preganglionic fibers*, to use Langley's term, make their exit exclusively in the white rami communicantes of the spinal cord (Gaskell), and all of them end with their terminal arborizations about ganglion cells situated at a greater or less distance from the cord. There are no connections between the separate ganglion cells either within the same or different ganglia.

The length of these fibers varies greatly (cf. Fig. 301, m_1—m_7). Some of them (m_1) end about the cells of the nearest ganglion, others (m_4, m_6) pass through several ganglia before reaching their endings, and by means of collaterals may therefore act upon a number of cells. Still others find their destination only when they reach ganglion cells situated far away in the periphery.

Postganglionic fibers (g, g_1, g_2, g_3, g_4) arise in the sympathetic ganglia and, without any connection with other ganglion cells, terminate, sometimes near, sometimes far away, in the free endings on smooth muscle cells, gland cells, etc. Langley believes that the course of each fiber or collateral is interrupted by one ganglion cell only. (See page 582 for Langley's use of nicotine in this connection.)

Part of the postganglionic fibers traverse the gray rami communicantes to the spinal nerves and reach their destination by these paths; part of them belong to branches which run an independent course to the periphery.

The plexuses of Auerbach and Meissner, found in the wall of the alimentary canal from the lowermost part of the œsophagus onward, which are commonly included in the sympathetic system, present some variations from the general behavior of the sympathetic nerves. For this reason they are set apart by Langley in a class by themselves. Nothing definite can be said at present as to their physiological status.

B. COURSE OF THE SYMPATHETIC FIBERS

According to Gaskell, the sympathetic trunk itself receives preganglionic fibers only from the first thoracic to the second to fourth or fifth lumbar roots. The cervical roots convey no visceral nerves; but visceral nerves are found in the first or second and third sacral. These latter do not unite with the sympathetic but contain fibers which are autonomic in function.

The preganglionic fibers belonging to the sympathetic unite either with cells in the ganglia of the sympathetic chain (lateral ganglia), or with cells in ganglia situated farther toward the periphery (collateral ganglia).

The following account of the course of pre- and postganglionic fibers and their connections, relating to the cat, is taken from Langley.

The cervical sympathetic receives fibers from the first to the seventh thoracic roots; in their exit from the spinal cord they are to a certain extent arranged according to their function. The most powerful effect on the dilator of the pupil is obtained from the first and second, on the nictitating membrane, on the eyelids, etc., from the first to the third, on the submaxillary glands from the second and third, on the vessels of the ear and the conjunctiva from the second to the fourth, on the pilomotor nerves of the head and neck from the fourth to the sixth. These details are mentioned because they are important for a proper conception of the regeneration phenomena to be described presently.

All these fibers terminate in the *superior cervical ganglion*, the cells of which send out postganglionic fibers to the plexuses about the blood vessels, to certain cranial nerves, and to the three upper cervical nerves. These joining the last named accompany their sensory branches to the skin and innervate the erector muscles of the hair, constituting therefore the pilomotor nerves.

The *stellate ganglion* receives fibers from the (third) fourth to the eighth (ninth) thoracic roots. Among its postganglionic fib [illegible] rs pass to the third to the eighth cervical nerves and the first to the third (fourth) thoracic nerves: they make their exit through the fifth to the eighth thoracic roots. Vasomotor and sweat nerves for the fore paw are contained in the fourth to the ninth thoracic roots. They unite with cells in the stellate ganglion, from which postganglionic fibers are given off to the brachial nerves, the latter like the pilomotor fibers running in the posterior branches of those nerves. This ganglion also sends accelerator nerves to the heart and possibly vasomotor nerves to the lungs; but it is not yet conclusively proved that these nerves actually proceed from cells in the stellate ganglion.

Those spinal nerve roots which send out fibers to the chain ganglia lying distally to the stellate ganglion, each supply three, four or more ganglia. The postganglionic fibers (pilomotor and vasomotor) unite with the corresponding spinal nerves and accompany their dorso-cutaneous branches to the skin.

The vasomotor and sweat nerves to the hind paw pass out probably in the twelfth thoracic to the second lumbar nerve roots; they unite with the sixth lumbar to the second sacral ganglia to be continued in the cutaneous branches of the spinal nerves.

The inhibitory and vasomotor nerves contained in the splanchnic are connected for the most part with cells in the solar plexus and have no relay station in the chain ganglia. They proceed from all roots between the fifth thoracic and second lumbar nerves.

The organs of the pelvis receive nerves both from the lumbar sympathetic and the sacral (cf. page 393). The former arise from all roots between the twelfth thoracic and fifth lumbar, and traverse the sympathetic cord either to the inferior mesenteric ganglion or to the sacral ganglia. Those entering the inferior mesenteric ganglion unite for the most part with its cells, but to a less extent also with ganglion cells situated in the peripheral organs. Most of the sympathetic nerves to the external genital organs are connected with cells in the sacral ganglia.

The autonomic fibers passing out through the first to the third sacral roots and uniting to form the nervi erigentes connect with the cells of ganglia strewn along their course and lying for the most part in the immediate vicinity of the organs for which they are destined.

GANGLIA OF THE SYMPATHETIC SYSTEM

SPINAL ROOT.		CERVICAL.	THORACIC.	LUMBAR.	SACRAL.
Thoracic	I	Sup. cerv.	....	....	....
	II	Sup. cerv.	....	....	....
	III	Sup. cerv.	....	....	....
	IV	Sup. and inf. cerv.	....	....	....
	V	Sup. and inf. cerv.	1, 2	....	....
	VI	Sup. (?) and inf. cerv.	1, 2, 3, 4, 5	....	....
	VII	Inf. cerv.	1, 2, 3, 4, 5, 6, 7, 8, 9	....	....
	VIII	....	? 5, 6, 7, 8, 9, 10, 11, 12	....	....
	IX	....	? 8, 9, 10, 11, 12	1, 2	....
	X	....	11, 12	1, 2, 3	....
	XI	....	12	1, 2, 3, 4	....
	XII	....	....	1, 2, 3, 4, 5	1
Lumbar	I	....	....	? 2, 3, 4, 5	1, 2, 3
	II	....	....	? 3, 4, 5	1, 2, 3, 4, 5

On the basis of his experiments upon animals and on the basis of comparative anatomy, Langley has constructed the above table illustrating the relations of the spinal roots to the ganglia of the sympathetic system in man. It will be observed that the main outflow of sympathetic fibers takes place between the first thoracic and second lumbar roots.

C. REGENERATION IN THE SYMPATHETIC NERVOUS SYSTEM

Regeneration in the sympathetic system is of particular interest because it is the only place in the entire nervous system where ganglion cells are found interpolated in the direct course of definite nerve fibers. As we have already seen (page 687) the fibers running in the cervical sympathetic which are interrupted by the superior cervical ganglion are distributed to the different spinal roots according to their destination. If now the cervical sympathetic is cut, after a time regeneration takes place just as in all the nerves. But what is specially remarkable in this case is this: that stimulation of the separate spinal roots after regeneration produces in the main the same effects as before they had been sectioned. Again, if the superior cervical ganglion be painted with nicotine after regeneration, we get the same negative results as if the painting were done previous to sectioning. *It follows that the regenerated nerve fibers have reëstablished their old connections, or have made new connections in the same ganglion with cells of exactly the same kind.* It would seem that the growing nerve fibers must be guided by some chemotropic influence to the very cells with which they were formerly connected (Langley).

By the same method Langley has found that postganglionic fibers likewise regenerate and reëstablish their old connections and that they also form new ones.

When the superior cervical ganglion is cut out, the cervical sympathetic does not recover its functions possibly because the preganglionic fibers are not capable of establishing functional connection with the peripheral tissues directly. We may suppose that the nutritive influence of the ganglion cell does not extend far enough to permit the fibers to grow farther than the interpolated ganglion. It is likewise impossible to bring about a union of the true efferent cranial or spinal nerve fibers with the postganglionic fibers, although union of these nerves with preganglionic fibers has often been demonstrated.

D. AFFERENT NERVES IN THE SYMPATHETIC

The sympathetic contains afferent fibers, whose trophic centers are for the most part in the spinal ganglia. The number of such fibers is much smaller than that of the efferent fibers. Thus Langley has found by the method of regeneration that only one-tenth of all the fibers in the hypogastric are afferent in function; in the nervus erigens the number is one-third.

Stimulation of any one of the white rami communicantes produces reflex movements and variations in the blood pressure. Hence they must contain afferent fibers. It appears that such fibers run almost exclusively to the thoracic and abdominal viscera, and that they probably have the same distribution as the corresponding efferent nerves. It is probable that they account for such conscious sensations as "referred pains," so called because they are referred to regions of the skin innervated from the same root as the diseased organ. Impulses from the latter are therefore conveyed in some way, either by mediation of the spinal ganglia or by mediation of the nerve cells of the spinal cord, to the sensory neurons of the skin.

For reflexes from the sympathetic ganglia, cf. page 583.

REFERENCES.—*Gaskell, Journal of Physiology,* vol. vii, 1886.—*Kocher,* "Mittheilungen aus den Grenzgebieten der Medizin und Chirurgie," vol. i, 1886. —*Langley,* several articles in the *Journal of Physiology,* vols. xii, xv, xvii, xviii, xix, xx, xxiii, xxv, xxvii–xxxi; 1891–1904.—*Langley,* "Ergebnisse der Physiologie," ii, 2, Wiesbaden, 1903.

CHAPTER XXVI

REPRODUCTION AND GROWTH

FIRST SECTION

REPRODUCTION

THE *physiology* of *reproduction* in general covers so wide a field and is related to so many branches of biology that even a superficial presentation of its most salient features would require more space than we have at our disposal. We shall therefore limit the discussion to those features of reproduction in man and the higher animals which are very important from the standpoint of human physiology, but which are not usually treated as belonging to the special province of embryology. The following brief survey of this field will indicate the scope we have in mind.

Reproduction in most of the higher animals is inaugurated by the *conjugation* of two different sexual elements, the male and the female. The female element, the *ovum*, is formed in the ovary: it was first demonstrated for the mammals by v. Baer in 1827. The male element, the *spermatozoon*, is formed in the testes and represents the "seminal bodies" discovered by Leuwenhoeck in 1677.

In mammals the spermatozoa are introduced into the female body by the act of *copulation*. If *fertilization* of the ovum then takes place, there develops within the female body a new individual, which, when it has reached a certain stage in its development, is expelled from the body of the mother. This latter process is called *birth* or *parturition*.

At birth the new individual is not developed far enough to seek independently and to utilize the ordinary food of the species, but must for a time derive its nourishment from the mother. The *milk glands* of the mother at this time are roused to a high degree of activity, and furnish a secretion, the *milk*, which contains in proper proportions the foodstuffs necessary for the maintenance of the newborn child.

The physiology of reproduction, as we shall limit the subject here, will accordingly include: *the functions of the male and female sexual organs, the processes of copulation and conception, birth, and the secretion of milk.*

§ 1. THE MALE SEXUAL ORGANS

These are: the *testes*, which produce the spermatozoa; the *accessory glands* (vesicular glands, prostate body, and the glands of Cowper), which produce secretions to be mixed with the spermatozoa in the seminal fluid; and the male organ, the *penis*, by which the seminal fluid is introduced into the female organs.

A. THE TESTES

Sexual maturity, or *puberty*, appears in the man at about the age of fifteen. The testes begin to increase in volume and to secrete seminal fluid. At the same time the foreskin becomes loosened from the glans penis, and the rest of the body exhibits many changes: the bones and the muscles become stronger (cf. below, page 709); the larynx increases in size, in consequence of which the voice becomes fuller and deeper, etc.

When the testes are removed by *castration* before sexual maturity, these changes do not take place—which proves clearly that they are occasioned by the testes.

The general character of the individual also is changed by castration, as may be seen best perhaps by comparison of the disposition of an ox with that of a bull. It follows that all the characteristics by which a man is distinguished from a woman depend essentially upon the testes and their activity (cf. also page 357).

The spermatozoa are minute bodies consisting of a thick head and a slender tail, which, in virtue of the whiplike movements of the tail, are capable of independent motion. The speed of their locomotion, considered with reference to their size, is rather high, namely, 0.05 to 0.15 mm. per second.

The spermatozoa are formed by a peculiar transformation of certain cells in the testes, known as *spermatids*. According to Lode, in 1 cu. mm. of human seminal fluid there are about 60,000 spermatozoa. The quantity of seminal fluid discharged at a single ejaculation may be estimated at about 3 cc.; whence the total number of spermatozoa in a single ejaculation would be in the neighborhood of 180,000,000—a perfectly enormous number in view of the fact that but a single spermatozoon is necessary for fertilization of the ovum.

Foges reports the interesting observation that the testis of a cock transplanted into the abdominal cavity will continue to produce spermatozoa, from which we may conclude that spermatogenesis is in part at least independent of the nervous system.

B. THE ACCESSORY SEXUAL GLANDS

In a castrated animal the *accessory glands* atrophy, showing that they must play some essential part in the sexual functions. If castration be performed before sexual maturity, they do not develop at all.

Nothing is known at present as to the special functions of the separate glands; but from the fact, established by comparative anatomical studies, that there is considerable variation in their relative sizes in different species, we may surmise that they all have an essentially common purpose.

The so-called *seminal vesicles* are not properly a receptacle for the seminal fluid, although they do always contain a greater or less number of spermatozoa: they produce a secretion of their own, which has led Owen to describe them as the vesicular glands. When they are extirpated either alone or in conjunction with the prostate body, sexual desire remains unimpaired, and copulation takes place in the same way as in the normal animal and with the usual frequency.

The fecundity of the animal, however, is very much reduced by the extirpation of the vesicular glands (in white rats) and if the prostate body be removed along with them, the procreative power is entirely lost. The accessory sexual glands therefore are *absolutely necessary* for the full fruition of the male sexual functions (Steinach).

Probably their most important purpose is to provide for the dilution of the testicular secretion—a condition which is indispensable for the motility of the spermatozoa. In the testis itself and in the epididymis where the fluid is thick the spermatozoa are not motile; but when semen from the testes is mixed with physiological salt solution, active movements appear wherever an actual mixing takes place (Iwanoff). The ova of rabbits, guinea pigs and dogs can be successfully fertilized by injecting into the vagina a mixture of sperm from the epididymis and physiological salt solution (Walker).

On the other hand it was found in Steinach's experiments that the spermatozoa remain motile in the prostate secretion from seven to ten times longer than they do in the physiological salt solution. This shows that the secretion contains other substances which have a favorable action upon the spermatozoa. Since acids are very harmful to the spermatozoa, it is possible that the secretion has the additional function of neutralizing any acid that may chance to be present in the vaginal mucus.

In the guinea pig and other rodents, the secretion of the vesicular gland coagulates in the vagina so as to form a plug which prevents the escape of the seminal fluid. This coagulation is caused by the action of an enzyme occurring in the secretion of the prostate (Camus and Gley).

The vasa deferentia in the cat receive their motor nerves from the (second) third to fourth (fifth) lumbar roots; these nerves have about the same peripheral course as the lumbar nerves to the bladder (Langley and Anderson; cf. page 393).

The vesicular glands of the guinea pig receive motor as well as secretory fibers by the hypogastric nerves; they leave the spinal cord in the second to the fourth lumbar nerves (Akutsu).

Mislawsky and Bormann state that the secretory fibers of the prostate run in the hypogastric nerves and that its muscles are supplied also with fibers from the nervi erigentes.

C. ERECTION AND EJACULATION

Just previous to the act of copulation the *penis* becomes rigid and erect, thus fitted to be introduced into the vagina. Friction of the glans against the walls of the vagina sets up a *reflex* by which the seminal fluid containing all the secretions of the accessory glands is discharged into the female organ (*ejaculation*). The rigidity of the male organ then passes off and the act of copulation is ended.

Erection is due to an in-rush of blood into the three cavernous bodies of the penis, caused by dilatation of its arteries under the influence of vasodilator nerves. These nerves (nervi erigentes) discovered by Eckhard and studied later by Lovén and others, leave the spinal cord in the anterior roots of the first to third sacral nerves, unite with the hypogastric plexus and run thence to the penis. They have their center in the lowermost part of the cord, so that erection can still be reflexly induced after section of the spinal cord between the dorsal and the lumbar regions (cf. page 588). In fact, at the moment of making such a section (in the guinea pig) erection and ejaculation occur (Spina).

According to L. R. Müller erection and ejaculation can be induced (in the dog) by rubbing the penis after extirpation of the lumbar and upper part of the sacral cord. It is likely therefore that the reflex can be mediated by peripheral ganglion cells.

Erection may be brought about also through the influence of higher nerve centers. Eckhard was able to induce the phenomenon in animals by the electrical stimulation of the cervical cord, of the pons, and of the crura cerebri. The fact that in man erection often occurs merely as the result of erotic ideas, is evidence that the nervi erigentes may be excited in the same way also by the cerebrum.

Stimulation of the nervi erigentes increases the volume of blood flowing through the pudenda interna vein beyond the mouth of the penis vein to about eightfold the volume flowing during the relaxed condition of the penis. Since, however, erection occurs as the result of the same stimulation the inflow of blood must be still greater. In erection as it occurs naturally the veins of the penis are compressed by contraction of the musculature about the urethra, thereby rendering the outflow of blood from the penis more difficult, which in turn serves to heighten the degree of erection. Compression of these veins alone however does not cause erection.

Erection obviously must be closely related to the functions of the testes; and yet observations on both men and animals go to show that erection is possible after castration and that sexual passion may not be entirely destroyed.

When ejaculation occurs, the seminal fluid is thrown by forcible contractions of the vasa deferentia into the urethra in the direction of the pars membranacea urethræ. Entrance to the urinary bladder is prevented chiefly by the sphincter of the bladder and by contraction of the musculature of the prostate.

The ejaculatory ducts open at the summit of the seminal eminence, while the mouths of the numerous ducts from the prostate are so arranged that they empty their secretion in exactly the opposite direction. When the semen pours out of the ejaculatory ducts, numerous streams of the secretion from the prostate are at the same time poured into the urethra and there results a very uniform mixture of the two fluids (Walker).

The seminal fluid is expelled from the urethra by contraction of the bulbocavernosus and the ischio-cavernosus muscles; according to Walker the sphincter urethræ membranaceæ should play an essential part in this also.

Ejaculation may take place without erection—in the guinea pig, for example, when the spinal cord is crushed by means of an exploring instrument. In the same animal Rémy found on the inferior vena cava at the level of the renal veins a small ganglion electrical stimulation of which produced a sudden ejaculation. Sexual desire was not destroyed by section of the nerves issuing from this ganglion, but erection and ejaculation were no longer possible.

§ 2. THE FEMALE SEXUAL ORGANS

A. THE OVARIES AND OVIDUCTS

The *primordial ova*, which are destined ultimately to become the mature ova capable of fertilization, are formed at a very early stage of intrauterine life. In the further course of development they become surrounded by a layer of germinal epithelial cells, the whole group being then known as the primary follicle.

From this primary follicle what is known as a *Graafian follicle* is developed in the following manner: The epithelium which surrounds the ovum begins to proliferate and becomes many-layered. Then in the space between these layers a fluid gradually collects, partly by transudation from the surrounding blood vessels and partly by disintegration of epithelial cells. In the human ovary this *liquor follicularis* is found only in that part of the follicle presenting toward the surface of the ovary. On the medial side of the follicle the epithelium forms a mass of cells surrounding the ovum and projecting into the follicular cavity as the *discus proligerus*. The follicle is also surrounded by a connective tissue envelope known as the *theca folliculi.*

At the same time the ovum, its nucleus (germinal vesicle) and nucleolus (germinal spot) grow in size and the ovum becomes surrounded by a membrane, the *zona pellucida*, secreted by the follicular epithelium. The membrane, however, is separated from the ovum by a small space.

In the further development of the ovum, the protoplasm from the center outward becomes transformed into *yolk spherules*, until finally there remains of the true protoplasm only a thin layer situated peripherally, and containing the nucleus.

Development of the primary follicle into the Graafian follicle takes place before sexual maturity, in fact before the birth of the young female. But the ova are not yet capable of being fertilized and will not be before the beginning of sexual maturity—i. e., about the fourteenth year. By this time the ova are about twice as large as when the Graafian follicle was formed, measuring now about 0.2 mm. in diameter, and have extruded from themselves half the *chromatin* (staining substance) of their nuclei.

When the follicle has reached a certain size, an internal proliferation in the inner layer of the theca folliculi takes place which finally leads to its rupture and to the consequent liberation of the ovum. The processes concerned in this, according to Nagel's description, shape themselves on this wise:

The vessels of the theca become strongly developed, and the cells about them multiply enormously. At the same time the protoplasm of the cells becomes filled with a material (luteïn) which gives the whole inner wall of the follicle a yellow cast. The *luteïn cells* become bulged out in the form of a papilla on the inner layer of the theca and this bulging continues, crowding the follicular contents more and more toward the thinnest part of the follicular wall turned toward the surface of the ovary, until finally the follicle bursts. Hand in hand with this proliferation of the luteïn cells there goes a fatty degeneration of the follicular epithelium, by which the ovum with its epithelium is released from the discus proligerus. The contents of the follicle are replaced in part at least by a blood clot: we then have instead of the Graafian follicle a *corpus luteum.*

Thus the ovum comes into the abdominal cavity and is ready to enter the *Fallopian tube* to be passed on into the uterus. The abdominal opening of the tube spreads out in the form of a funnel surrounded by fringelike processes known as *fimbriæ,* one of which, the *fimbria ovarica,* comes quite close up to the ovary. Along this fimbria, extending from the ovary to the tube, runs a groove, which, like the fimbriæ themselves and the mucous membrane lining the tubes, is clothed by a ciliated epithelium. These cilia beat in the direction of the tube, creating a current in the surrounding capillary spaces between the viscera, which probably plays a predominant part in guiding the ovum. The production of this current is materially aided by the peculiar position of the tube, its relation to the ovary being such as to form about the latter a sort of pocket, closed off from the abdominal cavity.

Once in the Fallopian tube the ovum is carried along to the uterus by the movements of the cilia. In this journey, which requires about three days, the remains of the follicular epithelium adherent to the ovum when it is set free, become stripped off, leaving the ovum naked.

It is probable that many of the ova set free from the ovary never reach the Fallopian tubes, but are lost in the abdominal cavity.

Opinions differ very much as to the time of ovulation (liberation of the ovum from the ovary), and a definite decision between them cannot be given at this time. Some authors suppose that it takes place only in connection with menstruation (before or after), others that it can occur at any time in connection with copulation.

B. THE UTERUS

The uterus is a hollow organ which serves the purpose of harboring the ovum during its development into the mature *fœtus* and of supplying the necessary nourishment for this development. The wall of the uterus consists externally of numerous smooth muscle fibers interlaced together, and internally of a mucous membrane lined with a ciliated epithelium, invaginations of which toward the muscle layer constitute the mucous glands. The cilia of the epithelium beat from above downward—i. e., from the fundus toward the mouth of the uterus.

The uterus differs radically from all other organs of the body in that its tissues undergo profound alterations under perfectly normal circumstances. Some of these alterations are related to menstruation, some of them to pregnancy.

By *menstruation* is meant a periodic discharge of blood from the uterus of the sexually mature female, which occurs about every twenty-eight days and continues on the average about four days. It begins at about the fourteenth year of age and constitutes the external sign of sexual maturity. The quantity of blood discharged at each period has been estimated at from 100–200 cc., but the amount is subject to great variations. At the age of forty-five to fifty years menstruation gradually ceases, and with it the ability to bear young is permanently lost. This age is designated as the *climacteric.*

It had long been supposed that menstruation was due to some nervous influence of the ovary over the uterus. But it has been observed that in monkeys menstruation can take place even when the ovaries have been removed from their normal position in the body and transplanted elsewhere, all nervous connections with the ovary being severed. Hence it is not improbable that the internal secretion of the ovary is the essential medium of influence (cf. page 358).

Just as in man, the appearance of puberty in woman is marked by other changes in the body: the mammary glands increase in size, the figure loses its childish delicacy and, by the deposition of subcutaneous fat, becomes more robust. Castration of the female (extirpation of the ovaries) likewise produces more or less sharply pronounced changes (cf. page 358).

The monthly changes in the uterus proceed as follows: five to ten days before the period of discharge the blood vessels of the mucous membrane become dilated, the membrane itself as a result swells up and a proliferation of its more superficial layers takes place. Then follows a hemorrhage in the subepithelial tissue which is probably not due to rupture of blood vessels, but to the escape from them of red blood corpuscles. The nutritive condition of the mucous membrane thus becomes impaired, and as a consequence its outermost layers (the *decidua menstrualis*) slough off (according to some authors the loss of the mucous membrane is not due to lack of nutrition, but to pressure of the escaping blood in the subjacent tissues); the period of discharge continues for about four days, when a process of restitution sets in. These changes proceed by a regeneration of tissue from the remaining epithelium and its invaginations, and last from five to ten days. Hence the tissue changes accompanying menstruation cover all told from fourteen to twenty-four days out of each month.

The physiological significance of menstruation probably consists in a preparation of the uterine wall for the reception of the fertilized ovum.

Like the rest of the mucous membrane of the uterus, that of the cervix bears on its surface a ciliated epithelium, invaginations of which form the cervical glands. These glands secrete a clear, viscid mucus which collects in the cervical canal soon after conception and remains there as a plug serving to keep the passage closed throughout pregnancy.

After the climacteric has been passed, and ova are no longer being formed, the mucous membrane of the uterus shrivels up, the connective tissue underlying it increases in quantity, the cervical glands atrophy, and the epithelium loses its cilia.

C. PREGNANCY AND BIRTH

Spermatozoa are independently motile, and in virtue of this property of motility can traverse great distances, relatively speaking. Their entrance into the uterus and Fallopian tubes is due no doubt to some *chemotactic* influence over them exercised by the secretions of those organs, and their ascent toward the ovaries within the tubes is traceable to their *rheotactic* properties (cf. page 56). Coming into contact with the ovum, the spermatozoon enters it, possibly under the spell of a *thigmotactic* influence (cf. page 56). Inside the ovum the spermatozoon produces changes comprehended under the term *fertilization*, which make it possible for the ovum to develop into a new individual.

When the ovum has been fertilized, it becomes attached to the mucous membrane of the uterus already prepared for it, and later becomes surrounded by the proliferating epithelium of the mucous membrane.

The material necessary for the nourishment of the ovum is received from the mother through the *placenta*. As the ovum grows the uterus increases in size, so that while before impregnation its capacity is 3–5 cc., at the close of pregnancy it is 5,000–7,000 cc. This colossal development produces remarkably little change in the organism as a whole, and the only permanent alterations remaining after pregnancy are certain folds in the subcutaneous connective tissue of the abdomen caused by the extreme tension to which it has been subjected, and certain anatomical differences in the wall of the uterus.

The *period of gestation* covers ten menstrual periods—i. e., about two hundred and eighty days—at the end of which time birth takes place.

The fœtus is discharged from the uterus by powerful contractions of its muscular walls, aided by simultaneous contractions of the diaphragm and abdominal muscles. The first effect of the uterine contractions is to draw the cervix on all sides tightly against the fœtus and to dilate the passage way until the child can be forced through. This stage of labor is called the *opening period*; that following, which terminates in the complete discharge of the offspring, is called the *expulsion period*. In cases of first births the former period lasts about twelve hours, in subsequent births six hours; the length of the expulsion period is estimated at two hours. These however are only average figures, and the duration of birth may vary considerably either way.

Owing to their painful character the contractions of the uterus in childbirth are commonly called *labor pains*. They are not continuous, but like the contractions themselves are intermittent and become progressively longer and more severe until near the culmination of labor.

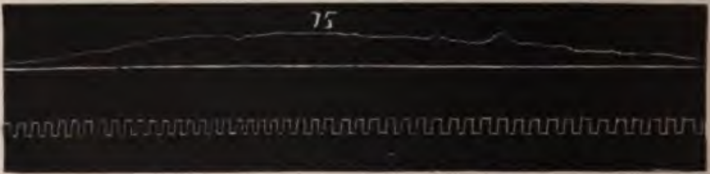

FIG. 302.—Normal curve of a contraction of the uterus, after Westermark. To be read from left to right.

The frequency of labor pains is variable. At the beginning of the first stage of labor, the interval between them is greatest, but it becomes steadily less until it reaches its minimum (less than one hundred seconds) at the end of this stage or some time during the second. When the pains are unusually long and severe, the pauses are also longer.

So long as there is no change in the volume of the contents of the uterus, the *intrauterine pressure* during the pauses, as estimated by Schatz, Polallion, Westermark, and others, remains remarkably even in any particular case of labor; but in different cases of labor it varies from 20 to 70 mm. Hg. When the amnion is ruptured a decrease in the volume of the uterine contents takes place, and this occasions a fall of the intrauterine pressure at the next pause. After this fall, however, the pressure during the following pauses tends to return to its original level, although that level is seldom reached, partly because the amniotic fluid escapes during each contraction of the wall, and partly because the child is pressed deeper and deeper into the pelvis, thus decreasing the volume of the uterine contents.

During a single pain the intrauterine pressure increases slowly at first, then rather rapidly, and finally slowly again until it reaches its highest point.

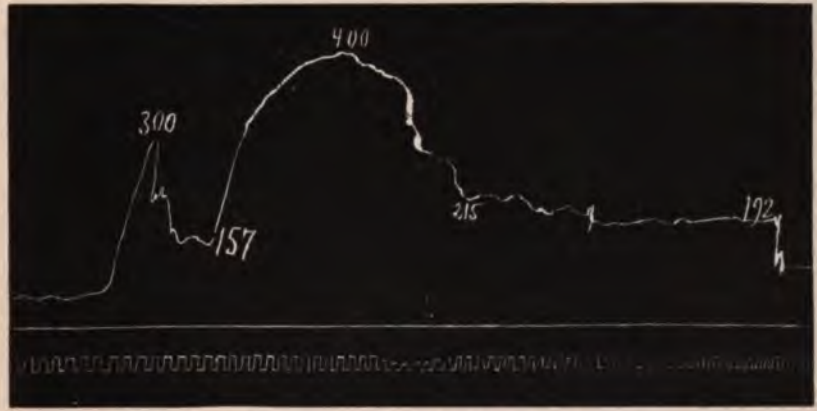

FIG. 303.—Pressure curve of the last contraction of the uterus in parturition, after Westermark. The high curve, reaching a pressure of 400 mm. Hg., represents the effect of the abdominal muscles. To be read from left to right.

For about eight seconds it remains at this maximum, after which it falls at first slowly, then for five to twenty-five seconds more rapidly and at the last very slowly (Fig. 302).

The highest pressure due to the contractions of the uterus alone, attained during the individual pains, increases during the progress of birth and reaches its maximum at the end. Out of 587 determinations made by Westermark the lowest was 20 mm. Hg., the highest 220, and the average 109 mm. The value naturally is considerably increased when the *abdominal pressure* also is brought to bear on the wall of the uterus. Especially is this the case during the last pains of the expulsive period, where values of 400 mm. Hg. have been observed (Fig. 303).

A short time after the birth of the child the placenta becomes loosened and with the amnion is expelled from the uterus as the *afterbirth*. The severe hemorrhage which occurs at first is stopped by the powerful contractions of the uterus. Then the organ gradually returns to its original size, the mucous membrane becomes regenerated, the muscle fibers decrease in length and breadth. Connected with these regeneration changes, which are complete after about two months, there is for a couple of weeks a discharge of a slimy, and at first bloody, material. The first menstruation however does not as a rule appear until about the tenth month, when lactation has ceased (cf. § 3).

D. INNERVATION OF THE SEXUAL ORGANS

Experimental data on the innervation of the uterus differ widely. While some authors state that the circular muscle fibers are innervated by the nervi erigentes and the longitudinal fibers by the hypogastric, Langley and Anderson have reached the conclusion that (in the rabbit and cat) only the lumbar nerves convey motor fibers and that these supply both the longitudinal and circular musculatures. The effect of unilateral stimulation is felt chiefly on the same side.

Nagel describes the innervation of the uterus *in the woman* as follows: one trunk arises from the hypogastric plexus, while others arise from the sacral nerves. The former receives fibers from the third sacral and sends a branch to the ureter. It then betakes itself to the cervical ganglion (plexus utero-vaginalis) which lies in the neighborhood of the lateral vaginal fold.

Besides this ganglion, which receives branches from the fourth sacral and is also connected with the hemorrhoidalis nerve, there are found in the vicinity of the ureter two other ganglia (the vesical plexus): the three ganglia are connected with one another and send branches to the uterus, the vagina, etc. Most of the uterine nerves come from these ganglia; a smaller part of them pass directly from the hypogastric plexus.

The nerves of the ovaries arise from the plexus renalis and from the lower portion of the plexus aorticus abdominalis.

The plexus surrounding the vagina arises from the cervical and vesicular ganglia, but also receives twigs from the third and fourth sacral nerves.

Movements of the uterus can be produced by stimulation of the different parts of the central nervous system (lumbar cord, medulla oblongata, anterior part of the optic thalami, cerebral cortex, probably the motor zone). But the uterus contracts spontaneously at a certain rhythm even when it is cut out of the body, and birth has been known to take place in a perfectly normal manner with all the uterine nerves cut (Rein) and after entire extirpation of the lower end of the spinal cord (Goltz and Ewald, cf. page 583). The central nervous system therefore plays a relatively unimportant part in controlling the movements of the uterus.

According to Keilmann and Knupffer, parturition takes place at once if the cervix be everted as far as the ganglion of the cervix. But Rein states that (in the dog) parturition takes place also after extirpation of the ganglion.

§ 3. SECRETION OF MILK

The newborn child is not far enough developed to seek and to take food without help. Its digestive organs are not yet capable of modifying the ordinary mixed diet of man, consequently nourishment for the child must be prepared for some months in the body of the mother. This is accomplished through the activity of the mammary glands which form and secrete the milk.

A. MILK

Milk constitutes the natural food of the child and hence contains in proper relative proportions all the foodstuffs necessary for the maintenance and development of the young body. We therefore find in milk proteid, fat, carbohydrate and mineral substances.

Among the *proteids of milk* we find: in small quantities lact-globulin, which is probably identical with serum globulin; lact-albumin, which is distinguished by certain properties from serum albumin; and, most important of all, *casein*. Cow's milk contains on the average about 3 per cent of casein and 0.5 per cent of other proteids.

Casein of cow's milk is a nucleo-albumin (cf. page 75) which is characterized chiefly by the fact that it coagulates under the influence of rennin (cf. page 250). In the dried state casein is a fine white powder. It is insoluble in water and very difficultly soluble in solutions of the common neutral salts, but in water to which a very slight trace of alkali has been added it is very readily soluble. It is soluble also in the presence of calcium carbonate from which the casein, acting as an acid, displaces the carbon dioxide. Its solutions do not coagulate on boiling and are not precipitated by magnesium sulphate, metallic salts, or mineral acids in excess.

The casein of woman's milk is distinguished from that of cow's milk chiefly in the form of the clot. While the clot of cow's milk is composed of dense, compact masses, in the coagulation of woman's milk a very loose and finely flocculent precipitate is formed. This difference, as will be readily understood, is a matter of great importance for digestion in the stomach of the infant. Besides, the casein of woman's milk does not always coagulate under the influence of rennin, and in its digestion, according to Kobrak, pseudonuclein is formed in very much smaller quantities than in digestion of cow's milk casein.

Various other circumstances point to the conclusion that the casein of woman's milk is a compound of a nucleo-albumin similar to the casein of cow's milk with a basic proteid body, probably a histon or a protamin. In fact it is possible to prepare from the casein of woman's milk a body which in its coagulation forms a compact cake not unlike that of cow's milk casein (Kobrak).

Finally, there has been found in woman's milk a proteid substance, very rich in sulphur and relatively poor in carbon, called opalisin (Wroblewsky), which occurs in cow's milk only in very slight quantities.

The *fat of milk* is present in the form of small droplets. For a long time it was believed with Ascherson that these droplets were surrounded by a proteid membrane (haptogen membrane). Later researches seemed to have shown that this is not true, but that the fusion of milk droplets is prevented only by the surface tension of the constituents of different specific gravity present in milk, or by a layer of casein or proteid solution held about the droplets by molecular attraction. But more recently the former view has been taken up again, and it is now stated very definitely by Voltz that the milk droplets possess envelopes of solid substance, which are probably true membranes. These envelopes contain both nitrogenous and nonnitrogenous compounds, as well as inorganic substances of which calcium is the chief. Their chemical composition varies greatly.

In woman's milk the fat droplets are larger and their number smaller than in cow's milk.

Butter, which is the fat of milk, consists mainly of palmitin and olein. Besides we find: stearic acid, myristinic acid, small quantities of butyric acid, caproic acid, etc., in the form of triglycerides. The melting point of the fat of woman's milk is 34° C., the congealing point, 20° C., and its specific gravity 0.966.

The most important *carbohydrate of milk is milk sugar* (cf. page 81).

Bunge has made the very remarkable observation that in dogs and rabbits the *mineral constituents* are present in the same relative proportion as in the ash of newborn animals, while the percentage composition of the ash of the blood and blood serum are quite different (cf. the following table).

ONE HUNDRED PARTS ASH CONTAIN	Suckling dog.	Dog's milk.	Dog's blood.	Dog's serum.	Young rabbit.	Rabbit's milk.
K_2O	8.5	10.7	3.1	2.4	10.8	10.1
Na_2O	8.2	6.1	45.6	52.1	6.0	7.9
CaO	35.8	34.4	0.9	2.1	35.0	35.7
MgO	1.6	1.5	0.4	0.5	2.2	2.2
Fe_2O_3	0.34	0.14	9.4	0.12	0.23	0.08
P_2O_5	39.8	37.5	13.2	5.9	41.9	39.9
Cl	7.3	12.4	35.6	47.6	4.9	5.4

This agreement is wanting, however, when we compare the composition of human milk with that of the ash of the human infant, as the following summaries of observations by de Lange, Hugonenq and Söldner will show.

ONE HUNDRED PARTS ASH CONTAIN	INFANT.				Mother's milk, average composition.
	Söldner, I.	Söldner, II.	Hugonenq.	De Lange.	
K_2O	8.9	6.8	6.2	6.5	30.1
Na_2O	10.0	8.3	8.1	8.8	14.8
CaO	33.5	38.7	40.5	38.9	15.6
MgO	1.3	0.6	1.5	1.4	2.8
Fe_2O_3	1.0	0.7	0.4	1.7	0.5
P_2O_5	37.7	40.2	35.3	37.6	16.3
Cl	8.8	6.6	4.3	6.3	20.1

Bunge refers this striking difference to the circumstance that the composition of milk ash agrees more closely with that of the ash of the young, the more rapidly the animal grows in weight after birth, pointing out that it is only by means of such an agreement that it would be possible for the rapidly growing animal to get every necessary mineral constituent in the proper proportion for its growth. In the slowly growing human infant this agreement is not necessary. But it is important that those constituents of the ash that serve to keep the composition of the urine normal should be supplied; hence the woman's milk is found to contain relatively more alkaline chlorides than the dog or rabbit milk.

In support of this view, Bunge compares the percentage composition of milk in tissue-forming substances, proteid and ash (calcium and phosphoric acid) in rapidly and slowly growing animals. It will be observed from the following table that these percentages are much higher in the former than in the latter.

Time in which the Newborn Offspring Doubles its Weight.		One Hundred Parts Milk Contain—			
		Proteid.	Ash.	Milk.	Phosphoric acid.
Man	180 days.	1.6	0.2	0.033	0.047
Horse..................	60 "	2.0	0.4	0.124	0.131
Cow	47 "	3.5	0.7	0.160	0.197
Goat..................	22 "	3.7	0.8	0.197	0.284
Sheep.................	15 "	4.9	0.8	0.245	0.293
Swine.................	14 "	5.2	0.8	0.249	0.308
Dog	9 "	7.4	1.3	0.455	0.508
Rabbit................	6 "	10.4	2.5	0.891	0.997

The average composition of cow's milk, taken from a very large number of analyses, is: 87.2 per cent water, 12.8 per cent solids, 3.0 per cent casein, 0.5 per cent albumin, 3.7 per cent fat, 4.9 per cent sugar and 0.7 per cent mineral constituents.

Woman's milk contains: 87–89 per cent water, 10.8–12.4 per cent solids, 1–2 per cent proteid, 3–4 per cent fat, 5–8 per cent sugar and 0.2–0.4 per cent mineral matter.

In general woman's milk is poorer in proteid and mineral constituents and richer in sugar and lecithin than cow's milk. The absolute quantity of milk secreted during the lactation period increases up to the twenty-eighth week, and then falls off. The *proteid content*, however, shows an almost constant decrease, as the following figures from Söldner will show. Part of the data are from different individuals.

Time after Delivery of Child.	Percentage of N.	Time after Delivery of Child.	Percentage of N.
5–6 days	0.327	20–21 days...........	0.218
8–9 "	0.247	29–30 "	0.180
9 "	0.235	74 "	0.153
9 and 11 "	0.278	113 "	0.152
4, 5, and 11 "	0.270	229 "	0.141
11 "	0.279		

The *fat content* likewise decreases somewhat in the course of the lactation period; but the *percentage of sugar* increases, at first pretty rapidly, then more and more slowly.

According to Bunge the mineral constituents of woman's milk have the following distribution per 1,000 parts: K_2O 0.703, Na_2O 0.257, CaO 0.343, MgO 0.065, Fe_2O_3 0.006, P_2O_5 0.469, Cl 0.445.

The quantity of milk secreted daily by both breasts of a nursing mother may be estimated at about 1,300 g., but this quantity is subject to great variations.

B. SECRETION OF MILK

The milk is secreted by the mammary glands. Each gland consists of 15–20 lobes grouped about as many ducts which open in the nipple. They are fully formed in the boy as well as in the girl at birth, and up to the end of the second to eighth week after birth they secrete a milky fluid called "witch's milk." In males the mammary glands as a rule become only slightly developed and never produce any secretion. In the female they begin at puberty to grow and increase considerably in size at that time. But a really important increase takes place only in connection with pregnancy. During the last few weeks of gestation, a fluid which differs considerably in composition from the milk and is known as the *colostrum*, is given off, and after birth has occurred the glands enter upon a period of vigorous activity which, with the child at the breast, continues for months. When the child is not nursed by the mother, the mammary glands atrophy and shrivel up to a small mass of connective tissue.

The nerves of the mammary glands end about the gland cells as a net of cirrous arborizations. In the human species they arise from the fourth to sixth intercostal nerves.

In animals the mammary glands are situated more distally and accordingly are supplied by more distal nerves. In the guinea pig, which has only a single pair of mammary glands, the nerves come from the spermatics. The five pairs of glands in the dog receive their nerves from this and several other nerve trunks.

The *influence of the nervous system* on the secretion of milk is a subject which has not yet been sufficiently investigated. From the observations of Goltz and Ewald on animals with the lower end of the spinal cord exsected (page 583), we learn that the mammary glands can secrete milk independently of the central nervous system. But the milk secreted by glands whose nerves have been sectioned exhibits morphological changes which go to show that the secretion is influenced in certain ways by the nervous system (K. Basch). Besides in the above experiments of Goltz and Ewald the influence of the peripheral sympathetic ganglia was not excluded.

Concerning the *mechanism of milk secretion*, the most divergent views have been expressed, and for the present we cannot decide whether the gland cells become disintegrated and contribute their own substance to the secretion, or whether they prepare the constituents of the milk from other materials. It seems, however, that there can be no very extensive destruction of cells, and the real question therefore narrows down to whether or not nuclei and protoplasm become *to some extent* transformed into secretion. Most recent writers on the subject think that this is the case; but that only the free end of the gland cell is lost, and that after the secretory products have in this way been discharged, a regeneration of the protoplasm from the basal, nucleated end of the cell takes place, and the same process of transformation, disintegration, etc., is repeated. For more detailed information we must refer to the literature bearing on the subject. Here we may only add that during lactation a varying number of leucocytes wander out of the interstitial connective tissue into the alveoli of the glands. It is possible that in the event of arrested lactation, they convey the fat away from the mammary gland.

Neither casein nor milk sugar is found in the blood; hence it is evident that they must be formed in the mammary gland itself.

K. Basch conceives that casein is formed by combination of a pseudonuclein, which is set free from the nuclei of the gland cell, with proteid. He bases this view on the fact, among other things, that by the action of a xanthin-free and sugar-free nucleic acid, prepared from the mammary gland, on the serum of ox blood, he was able to get a substance which had all the physical and chemical properties of cow's milk casein.

The percentage of fat in the milk can be raised by feeding fat. This increase is explained in different ways by different authors; but it is fairly probable that some of the fat of the food at least is carried over into the secretion. The fact that when iodized swine fat has been fed, it can be demonstrated in the milk in fairly large quantities (Winternitz) would favor this view. When iodine alone or potassium iodide is fed only the merest traces of iodine are found in the milk (Caspari).

On the other hand we have observations by Henriques and Hansen which indicate that the fat of the food in its passage through the cells of the milk glands suffers changes in its composition.

Even when an animal in lactation receives a diet which is poor in fat, the milk contains a considerable quantity of fat. In this case the milk fat must have been formed either from the carbohydrates fed or from the large deposits of fat in the body. This is demonstrated especially by the appearance of iodized fat in the milk at a time when there was no iodized fat in the food, but when iodized fat had previously been stored in the body (Caspari).

A cow on a restricted diet naturally secretes less milk than on a full diet; but the fat in her milk still has a lower melting point than the body's fat. This means that when the fat deposited in the body is called into requisition, relatively more olein is mobilized than palmatin and stearin (Henriques and Hansen).

It has ofttimes been confirmed that both the quantity of milk and the percentage of fat secreted increases on a diet which is rich in proteid, and this can only mean that proteid either directly or indirectly is a source of fat.

According to Thierfelder the sugar of milk arises from some mother substance not yet definitely identified, by the action of an enzyme associated with the gland cells.

The following may be mentioned here among the many different external agencies which influence the quantity and quality of the milk: (1) Frequent milking favors the activity of the glands. When the milking is done at stated intervals, the last milk stripped from the glands is richest in fat. This is probably due to the adherence of many fat particles to the walls between the folds of the mucous membrane as the earlier milk flowed through, the stripping process being necessary to dislodge them. (2) Too vigorous exercise diminishes the quantity of the milk, probably because the blood stream is diverted from the glands to the muscles. On the other hand, moderate exercise increases the secretion of milk in women, probably owing to its favorable effects on respiration, circulation, digestion, etc. (H. Munk).

SECOND SECTION

GROWTH OF THE HUMAN BODY

Several different periods may be recognized in the life of an individual human being. They are not marked off by sharply defined boundaries, so that one can say for example that on a certain day the individual is a youth and the next day a man or woman; but are recognized by the characteristics which plainly prevail, once they are fully established. These periods are:

(1) *Period of the Newborn,* from birth to the loss of the umbilical cord, which usually takes place in four or five days.

(2) *Period of Infancy,* up to the appearance of the first teeth, from the seventh to the ninth month.

(3) *Later Childhood,* up to the appearance of the permanent teeth about the seventh year.

(4) *Age of Boyhood and Girlhood,* up to the beginning of puberty, thirteenth to fourteenth years.

(5) *Age of Youth or Adolescence,* up to the time of bodily maturity, nineteenth to twenty-first year.

(6) *Age of Maturity,* up to the prime of life (climacteric in the woman), forty-fifth to fiftieth year.

(7) *Old Age.*

The first five periods are the ones of particular interest here because they cover almost the entire period of growth. The sixth period is the age within which man reaches his full physical and mental development. During the seventh period various disorders, caused more or less by chronic ailments of one kind or another, gradually encroach upon the normal functions, and the physical and mental powers are on the wane.

In turning now to the subject of the *size relations* of the body, let it be understood that the data presented are average results and that many individual variations from them are to be observed. In any exhaustive discussion of the subject it would be necessary to consider these variations and their meaning, but it will be impossible to do so here. The following is a concrete example of the method employed in arriving at average results.

Quetelet and Altherr carried out a series of observations on the weight of the newborn child, and found the mean value, irrespective of sex, to be 3,100 g. The extremes however were very considerable, for among the children weighed there were some under 1.5 kg., and some over 4.5 kg. In order to get a general view of the variations and thus to be able to grasp the significance of the mean value more correctly, the entire series of observations may be divided into groups according to weight: 1.0–1.5, 1.5–2.0, etc., and the proportion of individual cases belonging to each calculated in percentages of the entire number. We get in this way the following table, the results of which might be made still more clear by a graphic representation like that in Fig. 302.

BODY WEIGHT OF THE NEWBORN CHILD, IN KILOGRAMS.	Number of cases.	Percentage of cases.
1.0-1.5	2	0.33
1.5-2.0	8	1.34
2.0-2.5	54	9.01
2.5-3.0	180	30.05
3.0-3.5	251	41.90
3.5-4.0	88	14.69
4.0-4.5	15	2.51
4.5-5.0	1	0.17

The weight of the child at term is, on the average, 3,000–3,500 g. (extremes, 2,400–5,500). Boys are usually from 80 to 150 g. heavier than girls.

The length of the newborn child is, on the average, 50–51 cm. Boys appear as a rule to be 1 cm. longer than girls.

The weight of the newborn child increases with the number of pregnancies and with the age of the mother up to her fortieth year, as the following compilations by Ingerslew will show:

NUMBER OF THE PREGNANCY.	Weight of the child at birth, in grams.	AGE OF THE MOTHER.	Weight of the child at birth, in grams.
1	3,254	15–19	3,241
2	3,391	20–24	3,299
3	3,400	25–29	3,342
4	3,424	30–34	3,375
5	3,500	35–39	3,428
		40–44	3,326

The general physical condition and development of the mother also have much to do with the weight of the child. The greater the length of the mother's body, and the better its nutritive condition, the heavier and longer, generally speaking, will be the weight and length of the child at birth.

During the first two days after birth the child's body loses 100–200 g. in weight, but about the third day it begins to grow, and on the fifth to seventh day reaches its first weight again.

From this time on the growth in weight is very rapid, and by the twenty-fourth week it has doubled. At the end of the first year it is two and three-quarter times what it was at birth. The average monthly increase as given by Albrecht for the first twelve months is as follows: 900 g., 870, 870, 720, 600, 540, 420, 330, 330, 270, 240, and 210 g.; within the entire twelve months, therefore, a total of 6,300 g. is gained. Hence at the end of the year the weight is about 9,500 g.

The length of the infant's body at the end of five months is about 68 cm. and at the end of the first year about 77 cm. Growth therefore is more rapid at first than at any subsequent time.

The food of the child may be set down as the most important factor in determining the rate of growth during the first year. So far as we are able to judge from published observations on the subject, the child thrives better and its weight increases more rapidly when it is fed exclusively at the breast throughout the infancy period. This doubtless signifies that no artificial means of nourishment has ever been found which makes so little exactions on the delicate digestive apparatus as the mother's milk.

In three years the child's body has already reached half the length it will be when fully grown. During this period a boy will on the average have attained to a weight of 18–21 kg., and a girl, 17–21 kg.

The growth of the body in length during the later years of childhood will be evident from the following table:

Year of Age.	Boys: length in cm.	Girls: length in cm.
2	74.2	77.2
3	85.3	83.5
4	91.9	90.0
5	96.6	96.1
6	103.2	100.6
7	106.5	104.9

Obviously it is much more difficult to get an extensive series of observations on the growth of the child during the first five or six years of life than it is later. Within the years of seven and nineteen the material is much more accessible and the total number of observations on the rate of growth in length and body weight, made on children of school age by Bowditch in Boston, Key in Sweden, Kotelmann in Hamburg, Pagliani in Turin, Roberts in England and Porter in St. Louis, foots up a total of more than 125,000 individuals.

But we should not be warranted in drawing an average from all of this material taken together. There are certain racial characteristics which would need to be taken into account in so doing, and our purpose here will be better served if the material chosen be as homogeneous as possible. The observations of Key in Sweden probably fulfill this requirement as well as any.[1] It may be remarked however that the conclusions drawn from this material have been fully confirmed in the gross by observations in other countries. Certain age differences only are to be noted.

Fig. 304 represents, according to Key, the mean height and mean weight of male and female pupils in the higher schools of Sweden between the years of seven and twenty-one.

Up to and including the eleventh year boys are both taller and heavier than girls. From the twelfth year to the sixteenth this relationship changes: girls are then both taller and heavier on the average than boys. With the seventeenth year the relationship once more changes and the curve of development for boys rises above that for girls and the difference becomes greater and greater thereafter until complete maturity.

The *yearly increase in height and weight in boys* for the seventh year is 5 cm. and 2.3 kg., and for the eighth year, 5 cm. and 3.4 kg. For the ninth to the thirteenth year the growth in height by years is 4, 2, 3, 4, 4 cm., and the growth in weight by years is 1.7, 1.0, 1.9, 2.3, 3.1 kg. The growth in boys is at its feeblest during the twelfth and thirteenth years. With the fourteenth year the period of puberty is reached and the growth both in height and weight becomes much more rapid, the increase in the former for the fourteenth, fifteenth, sixteenth and seventeenth years being 5, 7, 6, 5 cm., and the increase in the latter being 4.7, 4.5, 5.5, 5.3 kg. respectively. The most rapid growth in height takes place earlier (fifteenth and sixteenth years) than the greatest growth in weight (sixteenth and seventeenth years). Since increase in weight is of greater significance than increase in height, the sixteenth and seventeenth years may be regarded as the years of most rapid physical development (cf. page 144).

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[1] Certainly much better than would observations made in any of the larger cities of the United States.—Ed.

After the seventeenth year the yearly rate of growth in height and weight is less, but the increase continues until about the twenty-first year, when the youth reaches his full physical stature. The height at this time is on the average 172 cm. and the body weight 65.2 kg. The man continues to grow, though very slowly, for several years more.

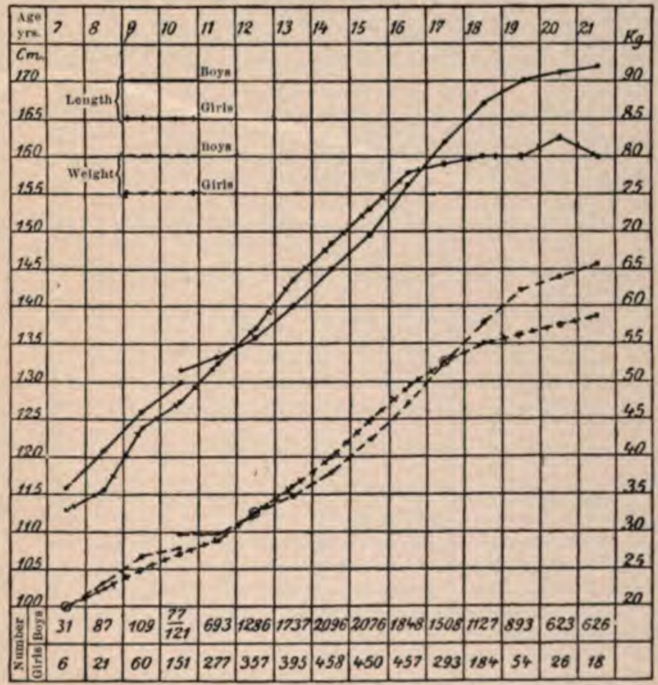

FIG. 304.—Curves representing the height and weight of boys and girls of different age, after Key.

The *physical development of girls* runs quite a different course. The period of feeble growth, which is so sharply marked for boys just previous to puberty, comes earlier for girls, namely, so far as concerns height, in the ninth year. The yearly increase in height of girls from the ninth to the seventeenth year is 7, 4, 5, 5, 6, 5, 4, 2, 1 cm. The increase in weight for the same years is 3.4, 1.9, 2.5, 2.5, 4.0, 3.7, 5.2, 4.1, 2.7, 3.0 kg. respectively. We see that there is a period in the development of girls also, from the ninth to the eleventh years inclusive, when the rate of growth in weight is relatively slow. The true puberty period, which is characterized by a rapid growth in weight, begins in the twelfth year and lasts until the fifteenth year (inclusive).

With girls the growth in height continues until only about the seventeenth year, while the increase in weight can be demonstrated up to the twentieth year.

From these and many other observations it follows that the physical development of girls is run through in less time than that of boys and that it terminates more abruptly.

Hand in hand with the more rapid development in height and weight during the puberty period, there goes also a correspondingly stronger development of the chest, as contrasted with the development during the years just preceding puberty. The mean increase in the chest measurement at the position of deepest inspiration, in boys from ten to seventeen years of age, is given by Kotelmann (for Hamburg) as follows: 1.68 cm., 1.97, 1.82, 0.99, 3.78, 3.47, 4.02, 2.44 cm. respectively.

According to Key's observations, the resistance of the body to harmful influences during the years just previous to puberty is relatively weak. But in the course of the puberty period, when the youthful life asserts itself in all its vigor, the resistance of the body increases, the percentage of sickness in the schools declines and reaches its minimum in the last year of this period (seventeen).

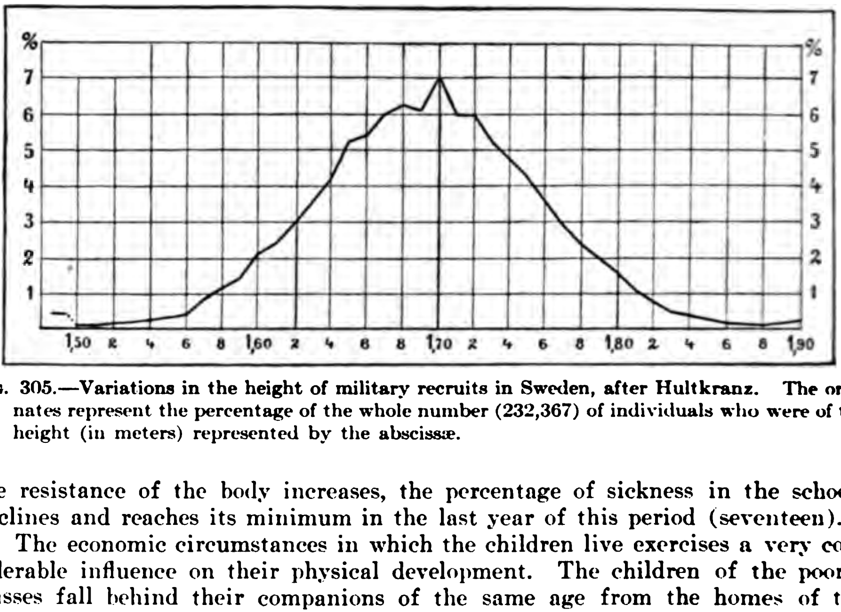

FIG. 305.—Variations in the height of military recruits in Sweden, after Hultkranz. The ordinates represent the percentage of the whole number (232,367) of individuals who were of the height (in meters) represented by the abscissæ.

The economic circumstances in which the children live exercises a very considerable influence on their physical development. The children of the poorer classes fall behind their companions of the same age from the homes of the well-to-do, both in height and weight. The period of feeble development just before puberty is longer for the poorer children. But once puberty begins, the period of rapid growth seems to proceed all the more rapidly in spite of its delay, and to terminate in the same year as for children of the well-to-do. The whole period is therefore shorter for poor children, but is characterized by an even more active development during its last years (Key).

Malling-Hansen has shown by a very extensive series of observations in Denmark that there is a *seasonal variation* in the rate of growth in children. From the end of November or the beginning of December to the end of March or the middle of April children grow very feebly—so much so that the increase in height is less than usual, however slow that may be. After this period of feeble growth follows a period during which growth in height is very active, but the increase in weight is reduced to a minimum. Indeed, children even lose in weight during this period of most active growth in height, almost as much as they have gained in the preceding period. This period lasts from March or April to July or August. Then follows a third period which continues until November or December. The increase in height is now very feeble, but the increase in weight rises rapidly and becomes considerable.

The *weight of the adult body varies greatly,* but may be estimated at 65–70 kg. for men and 56–60 kg. for women. At a mature age the weight in both sexes as a rule becomes greater by the deposit of fat.

The height of men of different nationalities is somewhat variable, as the following table compiled from average measurements of military recruits at the age of twenty to twenty-one years in the different countries will show:

Laplander		150.0	cm.
Hungarian		163.3	"
Bavarian		163.8	"
Russian		164.2	"
French		164.9	"
Italian (from different provinces)		156.0–166.5	"
Finlander (from different provinces)		165.9–169.9	"
English and Irish		169.0	"
Silesian		169.2	"
Dane		169.2	"
Norwegian	169.6	169.8	"
Scot		170.8	"
United States		173.3	"

Variations within the same nationality are considerable, as may be seen from Fig. 305. This represents, according to Hultkranz, the height of Swedes as determined by measurements of 232,367 military recruits made between 1887 and 1894.

We have no measurements similar to these for women but from observations which have been made, we may say that, on the average, a grown woman is about 12 cm. shorter than a grown man.

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INDEX

Abdominal pressure, 299, 699.
Abdominal type of respiration, 317, 318, Fig. 126, A.
Abdominal viscera, vasomotor nerves of, 233, 235.
Abducens nerve, 680.
Aberration, chromatic, 526, Fig. 221.
  spherical, 223, 522, Fig. 218.
Absorption, 31, 35, 301.
  from serous cavities, 353.
  influence of stimulants on, 302.
  of carbohydrates, 303.
  of fats, 304.
  of gases, by liquids, 334.
    by naked cells, 31.
  of iron, 307, Fig. 119; 308.
  of mineral substances, 308.
  of proteid, 305.
  of water, 302.
  relative power of, in different divisions of the alimentary canal, 302.
Accelerator nerves of heart, 191, 688.
Accessory sexual glands, 691, 692.
Accommodation in vision, 529.
  center for, 535, Fig. 230.
  mechanism of, 530 seq.
    protrusion of iris, 531, Fig. 226.
    reflected images, 531, Fig. 225.
    structure of ciliary muscle, 532, Fig. 227.
    theory of Helmholtz, 533.
    theory of Schön, 534, Fig. 229.
    zonule of Zinn, 533, Fig. 228.
  range of, 529, 530.
Acerebral rigidity, 616.
Acetic acid, 384.
Aceto-acetic acid, 376.
Acetone bodies, 376, 384.
Achroödextrin, 246.
Acids as excitants of pancreatic secretion, 269, 270.
Acid albumin, 292.
Acid albuminate, 74, 249.
Acid equivalent of fats, 79.
Acid of gastric juice, 247.
Acid sulphur, 373.
Acid taste, 484.
Actinia, 56.
Action currents, defined, 48.
  in glands, 48.
  in heart, 13, Fig. 13; 179, Fig. 63; 180, Fig. 64.
  in muscle and nerve, 48, 410, 431.
  in plants, 49, 50.
Activation of oxygen, 19, note.
  of zymogen, 38.
Active movements, perception of, 471.
Adamkiewicz's reaction for proteid, 73.
Adaptation of eye to different lights, 540.
Adelomorphous secreting cells, 266.
Adenin, 76, 372.
Adolescence, period of, 706.
Adrenal bodies, internal secretion of, 364 seq.
Adrenalin, 366.
Afferent and efferent nerves, 564, 565.
Afferent and efferent pathways in cord, 591, 592, 593, 595, 596.
Afterbirth, 699.
Afterbrain or myelencephalon, 600, 602.
After extension of muscle, 412.
After-image, negative, 539.
  positive, 538.
After-loading of muscle, 435.
After shortening of muscle, 412.
Age, changes due to, 66.
  influence of, on metabolism, 120.
  influence of, on rate of heart beat, 197.
Agglutination, 149, 156.
Agraphia, musical, 665.
Air, alveolar, exchange of, with blood, 340.
  atmospheric, composition of, 334, 342.
  changes produced in, by respiration, 342.
  complemental, residual, etc., 320.
  exchange of, in lungs, 319.
  expired, 342.
    explanation of evil effects of, 345.
    poisonous gases in, 344.
Air pressure, influence of, on number of corpuscles, 149.
Air pump, 334.
Air space, noxious, in lungs, 320.
Air-transmission, method of recording by, 11.
Alanin, 70, 373.
Albuminates, 74.
Albumins, properties of, 73.

Albuminous glands, 261.
Albumoid, 78.
Albumoses, 74, 249.
  food value of, 108.
  influence of, on coagulation, 159.
  poisonous effects of, 250.
  primary and secondary, formed in digestion, 249.
Alcohol, food value of, 110.
  formed in body, 376.
Alcoholic fermentation, 28, 40, 80.
Alcoholism, 30.
Aldehyde, glycerin, 373.
Alexia, or word blindness, 663, 669.
Algæ at high temperature, 29.
Alimentary canal, digestion in different divisions of, 290.
  movements of, 278.
Alimentary glycosuria, 127, 363, 374.
Alkali albuminates, 74.
Alkaline taste, 484.
"All or none" law, 183.
Allantoïn, 373, 382.
Alloxuric bases, 76; see also *Purin bases.*
Alveoli, exchange of gases in, 340.
  partial pressure of gases in, 341.
Amacrine cells, 515, Fig. 211.
Amblystoma, 59, 60.
Amino acids, part played by, in synthesis of proteid, 23.
  as products of digestion, 249, 255.
  as a source of urea, 370.
Amino-acetic acid, 70.
Amino-butyric acid, 70, 72.
Amino-caproic acid, 70.
Amino-ethyl-sulphonic acid, 253.
Amino-propionic acid, 70.
Amino-pyro-tartaric acid, 70.
Amino-succinic acid, 70, 110.
Amino-valerianic acid, 70, 72, 249.
Ammonia, formation of, in body, 370.
  in expired air, 345.
  in urine, 372, 382.
Ammonium carbamate, 370.
Ammonium carbonate, 370.
Ammonium isocyanate, 381.
Ammonium lactate, 371.
Amnestic aphasia, 662.
Amœba, ingestion of food by, 36.
  movements of, 42.
  under low temperature, 29.
  protoplasmic currents in, 43, Fig. 26.
  successive phases in life of, 36, Fig. 21.
Amœba polypodia, 35, Fig. 20.
Amphibolous biliary fistula, 243.
Amphioxus, functions of "brain of," 618.
Ampulla of semicircular canal, 474.
Amusia, 665.
Amylolytic enzyme, 243.
Amylolytic enzyme, in the bile, 254.
  in the pancreatic juice, 251.
  in the saliva, 246.
Anæmia, effect of, on fatigue, 445.
  of brain in sleep, 677.
  on power of localization, 464.
Anaerobic bacteria, 28.
Anæsthesia, 360, 597.
Anagyrin, producing vasoconstriction, 583.
Analysis of sound, 493.
Anatomy, comparative, 2.
Anelectrotonus, 425, Fig. 162.
Angle α, 525.
Angle of incidence, 509, Fig. 206.
  of refraction, 509, Fig. 206.
  visual, 518.
Angular convolution, 639, Fig. 289.
Animal diet, 145.
Animal gum, 82.
Animal heat, relation of muscular activity to, 116; see also *Heat production.*
Anisotonic solutions, 32.
Anode, reduction of excitability by, 425.
  stimulating effect of, 59, 424.
Answering organ, defined, 411.
Antagonistic muscles, inhibition of, by stimulation of cortex, 636, 640.
Antennularia antenina, 64, Fig. 37.
Anterior columns of spinal cord, 562, Fig. 254.
Anterior horn of spinal cord, 563.
Anterior roots of spinal cord, 563, 566, 593.
Antero-lateral columns of spinal cord, 595.
Anthrax bacillus, ingestion of, 37, Fig. 22.
Anthrax spores, survival of, at low temperature, 29.
Antibodies, 156.
Antienzymes in blood, 155.
  in organs, 269.
Antilytic effect in blood, 157.
Antiperistalsis, 289, Fig. 117.
Antiprecipitating effect in blood, 157.
Antiseptic methods, 5.
Antitoxin in blood, 156.
Antrum pylori, 283.
Anus, innervation of sphincters of, 299.
Anvil of ear, 495, Fig. 197; 496, Fig. 198.
Aorta, 162.
  blood pressure curve in, 170, Fig. 57; 171, Fig. 58.
  cubic enlargement of, 201.
Apex beat, 172 seq.
  curve of, in horse, 173, Fig. 60.
  schema illustrating Ludwig's theory of, 172, Fig. 59.
  time relations of, in man, 175, Fig. 62.
Aphasia, 663.
  alexia (word blindness), 663, 669.
  amnestic, 662.
  motor, 663.

Aphasia, sensory, 664.
  vocal motor, 665.
Aplysia, 35.
Apnœa, 332
  true and false, 333.
Apparatus figured
  Circulation:
    capillary pressure, 221, Fig. 91.
    cardiograph, 174, Fig. 61.
    hæmodromograph, 209, Fig. 81.
    heart sound, 168, Fig. 55.
    manometer, elastic or membrane, 9, Fig. 5.
    manometer, mercury, 8, Fig. 3.
    plethysmograph, 211, Fig. 83.
    sphygmograph, 215, Fig. 87.
    sphygmomanometer of Erlanger, 203, Fig. 76.
    stromuhr, 209, Fig. 80.
  General methods:
    electric signal, 10, Fig. 7.
    kymograph, 6, Fig. 1; 9, Fig. 6.
    recording tambour of Marey, 11, Fig. 9.
  Muscle and nerve physiology:
    capillary electrometer, 13, Fig. 12.
    elasticity apparatus, 412, Fig. 151.
    ergograph, 444, Fig. 179.
    induction coil, 420, Fig. 158.
    muscle lever, 6, Fig. 1.
    nonpolarizable electrodes, 419, Fig. 157.
    rheocord, 418, Fig. 156.
    rheotome, 432, Fig. 169.
    tension recorder, 414, Fig. 153.
    Wagner hammer, 421, Fig. 159.
  Metabolism:
    face mask, 85, Fig. 39.
    respiration calorimeter of Atwater and Benedict, schema, 86, Fig. 40.
    of Sondén and Tigerstedt, 88, Fig. 42.
    of Voit and Pettenkoffer, 87, Fig. 41.
  Respiration:
    air-pump of Ludwig, 334, Fig. 130.
    illustrating experiment with rabbit's lungs, 311, Fig. 120.
    lung catheter, Ludwig's construction, 341, Fig. 133.
    registering volume of expired air, 313, Fig. 122.
    spirometer, 320, Fig. 128.
  Special senses:
    black and white discs, 539, Fig. 233.
    entoptic phenomena, 521, Fig. 216.
    olfactometer of Zwaardemaker, 487, Fig. 192.
    resonator of Helmholtz, 493, Fig. 195.
    siren of Seebeck, 490, Fig. 193.
    stereoscope of Brewster, 558, Fig. 251.
Appetite, importance of, in indigestion, 263, 264, 290.
Aqueduct of Sylvius, 614.
Aqueous humor, 508, 509.
  refractive index of, 512.
Arabinose, 81.
Arcellæ, motility, 45.
Arenicola cristata, effects of salts on larvæ of, 25.
Arginin, 70, 255.
Argon in blood, 335,
Aromatic oxyacids, 378.
Arterial blood, gases in, 339.
  tension of carbon dioxide and oxygen in, 341.
Arterial pulse, 212; see also *Pulse.*
Arteries, 161.
  blood pressure in, 204.
  coronary, 180.
  cubic enlargement of, 201, Fig. 75.
  elasticity of, 200, 201.
  flow of blood in, 200.
  innervation of, 231, 234.
  movements of blood in, 218.
  resistance in, 205.
  resistance of, to rupture, 201, 202.
  velocity of blood flow in, 209.
Arterin, 150.
Ascaris, anaerobic mode of life of, 27.
Ash constituents, see *Mineral substances* and *Inorganic substances.*
  absorption of, 307.
  in blood, 154.
  in food, 83.
  in milk, 702.
  in urine, 384.
Asparagin, food value of, 110.
Aspartic acid, 70, 72, 249, 370.
Asphyxiation, 333, 396, 580.
  resistance of different nerve cells to, 573, Fig. 257.
Aspiration of thorax, 310, 311; see also *Suction in thoracic cavity.*
  effect of, on veins, 223.
Assimilation, 22, 26.
Assimilative processes induced by stimulation, 62.
Association centers of Flechsig, 665 seq.
  anterior, 668.
  coöperation of, with sensory areas, 670.
  mechanics of, 670–673.
  middle, 668.
  posterior, 669.
  seat of organized memory in, 671.
Association fibers, 663, 664, 668.
Association pathways, 664, 670.
Astasia, 607.
Asterina, 56.
Asthenia, 607.
Astigmatism, 522, 524, Fig. 219.
  correction of, 525.
Ataxia, 472.

Ataxia, cerebellar, 611.
Atmospheric air, 334; see also *Air*.
Atonia, 607.
Atrio-ventricular valves, 165, 166, Fig. 54.
Atrophy, 448.
Atropine, formation of urine and, 389.
  secretion of saliva and, 258.
Auditory area of cortex, 654, Fig. 293.
Auditory meatus, external, 494, Fig. 196.
Auditory nerve, 681.
  excitation of, 498 seq.
Auditory ossicles, 495.
Auditory sensations, 489.
Auerbach's plexus, 284, Fig. 114; 288, 687.
Augmentation of reflexes, 579.
***Aurelia*, osmotic relations in, 34.**
Auricle, 161; see also *Heart*.
  in cardiogram, 173, Fig. 60.
  maximum pressure in, 169.
  negative pressure in, 177.
  time relations in, 173, Fig. 60.
Autochthonous fibers, 575.
Autointoxication, 295.
Autolytic processes, 38.
Automatic excitation, 52, 356, 570, 580.
Automatism of the heart, 185, 186.
Autonomic nervous system, 686.
Auxotonic contraction, 435, 436.
Avidity of two acids for a base, 338.
Axis cylinder processes, 559.
Axis of rotation of the eye, 549; 550, Fig. 240.
Axis, visual or optical, 513, Fig. 210; 525.
Axon reflex, 584, Fig. 258.
Axons, 559.
Azobacteria, 24.

Bacillum volutans, 55.
Bacillus typhosus, 156.
Bacteria, anaerobic, 28.
  decomposition of proteids by, 250.
  in the blood, 155, 156.
  in the intestine, 295, 297.
  in the respiratory passages, 323.
  in the stomach, 247, note; 291.
  production of light by, 45.
Bacterium photometricum, 57, Fig. 33.
Bacterium phosphorescens, 29.
Basal ganglia of the brain, 632.
Basilar membrane, organ of Corti, 499; 500, Fig. 199.
Bathmotropic effect of vagus, 189.
Beats in musical sound, 501.
Becquerel rays, 58.
Bell's doctrine, 566.
Benzoic acid, 378.
Benzoyl-glycocoll, 378, 383.
Bilateral movements from stimulation of cortex, 640.
Bile, 253.
  absorption of, from intestine, 273.
  antiseptic properties of, 298.
  circulation of, 273.
  composition of, 254.
  digestion after exclusion of, 296.
  discharge of, into intestine, 275, Fig. 110.
  enzymes in, 254.
  excretory products in, 254.
  influence of, on amylolytic digestion, 251.
  influence of, on tryptic digestion, 294.
  reabsorption of, from lymphatics, 275.
  secretion of, 272.
    dependence of, on blood supply, 273.
    specific excitants of, 275.
  solubility of fatty acids in, 254, 296.
Bile acids, 253, 384.
Bile pigments, 253.
  in urine, 384.
Bile salts, 253, 254.
Biliary ducts, 275.
Biliary fistula, 243, 298.
Biliprasin, 253.
Bilirubin, 253.
Biliverdin, 253.
Biliverdinic acid, 254.
Binocular field of vision, 551; 552, Fig. 242.
Birds, extirpation of cerebrum in, 622.
  extirpation of liver in, 371.
Birth, 697.
Bitter taste, 484.
Biuret reaction, 73.
Bladder, gall, 275.
  urinary, 391.
Blind spot, 516.
Blood, 147.
  amount of, in body, 148.
  amount of, supplied to different organs, 240
  antitoxins in, 156.
  bacteriocidal action of, 156.
  coagulation of, 147, 154, 157.
  constituents of, 147.
  constitution of, variable according to organ 157.
  corpuscles of, red, 148, 150.
    white, 153.
  cytolytic action, 156.
  distribution of, in body, 239.
  effect of condition of, on respiratory center, 331.
  enzymes in, 155.
  gases in, 335.
  general survey of movements of, 161.
  menstrual, 696.
  precipitins in, 156.
  quantitative composition of, 154.
  quantity of, supplied to different organs, 240.
  reaction of, 147.
  in urine, 384.

Blood, viscosity of, 222.
Blood corpuscles, red, 148, 150.
  chemical composition of, 150, 152.
  destruction of, 150, 368.
  dry substance in, 149.
  formation of, 150.
  gases in, 336, 338.
  hæmoglobin content in, 152.
  movements of, in capillaries, 221.
  nuclei of, 17.
  number of, 149.
  percentage of, in whole blood, 149.
  permeability of, 33.
  specific gravity of, 149.
  stroma of, 150.
Blood corpuscles, white, 153; see also *Leucocytes*.
Blood crystals, 150, Fig. 46; 153, Fig. 49.
Blood flow in arteries, 200, 218.
  in capillaries, 219.
  in veins, 223.
  muscular work and, 449.
  through coronary vessels, 180.
  through heart, 165.
  velocity of, in arteries, 209.
      in diastole and systole, 210.
      variations of, in man, 212.
    in capillaries, 221.
    in veins, 224.
Blood gases, 333.
  distribution of, between corpuscles and plasma, 340.
  methods of determining, 335, 341.
  quantity of, 339.
  tension of, 341.
Bloodletting, 208.
Blood pigments, 150, 152; see also *Hæmoglobin*.
  in urine, 384.
Blood plasma, 154.
Blood platelets, 153.
Blood pressure, 202.
  comparative, in arteries of different sizes, 208.
  curves of, 8, Fig. 4; 205, Fig. 77; 206, Fig. 78; 207, Fig. 79.
    in left ventricle and aorta, 171, Fig. 58.
    intracardial, 169, Fig. 56.
      compared with apex beat, 173, Fig. 60.
  effect of adrenalin on, 366.
  effect of, on heart, 171.
  effect of vagus stimulation on, 205, Fig. 77; 206, Fig. 78; 207, Fig. 79.
  factors determining, 204, 205, 206.
  fall in, 206, Fig. 78.
  heart frequency and, 205.
  height of, 204.
  in arteries, 204, 208.
  in capillaries, 219, 221, Fig. 91.
Blood pressure in muscular work, 449.
  in pulmonary vessels, 228, 229.
  in veins, 223.
  maximum systolic, 204.
  minimum diastolic, 204.
  reflex fall in, 237, Fig. 98.
  reflex rise in, 236, Fig. 97.
  regulation of, 194, 219.
  regulation of respiratory variations in, 230.
  respiratory variations in, 229.
Blood serum, 154, 155.
  agglutination of Bacillus typhosus by, 156.
Blood supply to brain, 676.
  to different organs, 240.
  to heart, 180.
Blood volume, influence of, on blood pressure, 206.
Bodily movements, see *Muscular work*.
  influence of, on blood pressure, 449.
    on metabolism, 108, 110, 123.
    on pulse rate, 197.
    on respiration, 318.
    on storage of proteid, 63.
Body, human, chemical constituents of, 68.
  distribution of blood in, 239.
  growth of, 705.
  influence of attitude of, on blood flow, 226, 227.
  height of adult, 711.
  weight of, 96, 711.
  temperature of, 398; see also *Temperature of body*.
Bones, destruction of, in starvation, 98.
  conduction of sound through, 494.
Bony fish, extirpation of cerebrum in, 619.
Boyhood, age of, 706.
Boys, growth of, 708, 709, Fig. 304.
  nutritive requirements for, 144.
Bowman's capsule, 385, Fig. 144; 386.
Brain, as organ of the mind, 629, 670.
  blood supply to, 676.
  divisions of, 600, Fig. 267.
  fatigue and recovery in, 676, 677.
  influence of anterior parts of, on respiration, 329.
Brain of *Amphioxus*, 618.
  of bony fish (*Squalius cephalus*), 618, Fig. 274.
  of dog, 624, Fig. 280; 625, Fig. 281; 632, Fig. 282.
  of dog shark (*Scyllium canicula*), 619, Fig. 275.
  of lizard (*Hatteria punctata*), 621, Fig. 277.
  of pigeon, 622, Fig. 278.
  of rabbit, 623, Fig. 279.
  principles of interpreting results in study of, 601.
  temperature of, 678.

Brain-stem, functions of, as a whole, 618 seq.
  methods of study of, 599.
  physiology of, 599.
Breath volume, 319.
Brightness, highest in spectrum, 541.
Broca's area, 631, 662, Fig. 296.
Broca's convolution, 664.
Bronchial muscles, 324.
Bronchial sound, 322.
Brunner, glands of, 255.
Burdach's column, 591, Fig. 264; 592.
Butter, 701.
Butyric acid, 701.

C:N ratio in fæces, 90.
  in proteid, 92.
  in urine, 90.
Cadaverin, 249.
Cæcum, 289, 298.
Calcarine fissure, 639, Fig. 290; 657.
Calcium, absorption and excretion of, 133.
  effect of, on heart, 25.
  in coagulation, 158.
    on muscular movements of larvæ, 25.
    on skeletal muscles, 25.
    on smooth muscles, 25.
  hunger, 98.
  importance of, in plant, 24.
  in milk of cow, 351; see also *Milk, composition of.*
  rennin and, 250.
  salts of, certain ones favorable for higher animals, poisonous for unicellular, 26.
Calcium chloride, 25.
Calcium oxalate formed in cells, 41.
Calorie, definition of, 26, note.
Calorimetry, direct and indirect, 94.
Cane sugar, 81, 126, 127, 251, 255.
Capillaries, blood flow in, 219.
  blood pressure in, 221.
  contractility of, 220, Fig. 89.
  lymph formation from, 350 seq.
  nerves for, 221.
  stimulated and not stimulated, 220, Fig. 90.
  structure of, 220.
  velocity of blood flow in, 221.
Capillary electrometer, 13, Fig. 12.
Caproic acid, 701.
Capsule, internal, 647, Fig. 292.
Carbamic acid, 155, 370.
Carbamide, 381; see also *Urea.*
Carbohydrate group in nucleic acid, 77.
Carbohydrate groups in proteid molecule, 71.
Carbohydrates, absorption of, 303.
  chemical nature of, 80.
  decomposition of, 374.
  determination of, in food, 84.
  digestion of, in stomach, 291.
  formation of glycogen from, 374, 375.
Carbohydrates formed from proteid, 127, 373.
  in blood, 155, 374.
  in intestines, 297.
  influence of, on metabolism, 105.
  influence of pancreas on metabolism of, 364.
  metabolism, total, according to supply of, 106.
  metabolized before fats, 105.
  metabolized in muscular work, 113.
  quantity of, in diet, 142.
  relation of, to proteid retention, 121.
  specific need of body for, 128.
  storage of, in body, 124, 364.
  utilization of, 139.
Carbolic acid, effect of, on nervous system, 574.
Carbon, channels of excretion of, 89, 90, 342, 397.
  in expired air, 89.
  in fæces, 90.
  in urine, 89.
Carbon dioxide, absorption of, by hæmoglobin, 339, Fig. 132.
  coefficient of absorption of, 338.
  determination of, in metabolism, 85 seq.
  diurnal variations of, 344, Fig. 135; 345, Fig. 136.
  effect of, on respiratory center, 332.
  elimination of, by young, 118, 143.
    daily, per hour, 346.
    through skin, 397.
  formation of, in nerve, 434.
  in atmospheric air, 342.
  in blood, 337.
    combination of, 337.
    distribution of, between corpuscles and plasma, 340.
    influence of, on absorption of oxygen, 337.
    percentages of, in arterial and venous, 339.
    tension of, in blood and lungs, 341.
  increased output of, in fatigue, 446.
  in expired air, 89, 342, 343.
  in lymph, 348.
  production of, by animals and plants, 27.
  reduction of, by chlorophyll, 23.
  tension of, in tissues, 342.
Carcinus (green crab), osmotic pressure in, 34.
  neurofibrils in, 560.
  reflex movements of, 585.
Cardia of stomach, 282.
  innervation of, 284, Fig. 114.
  opening of, in deglutition, 282.
Cardiac inhibitory center, resistance of, to

Ca

Cardinal points of eye, 512; 513, Fig. 210.
Cardiogram, 173, Fig. 60; 175, Fig. 62.
Cardiograph, 174.
Cardiographic sound, 168, Fig. 55.
Carniferrin, 307, Fig. 119.
Carnin, 413.
Carnosin, 413.
Casein, coagulation of, in stomach, 250.
  digestion of, 255, 291.
  formation of, 705.
  of woman's and of cow's milk, 701.
  percentage composition of, 82.
  trypsin and, 252.
Castration, 357, 358, 367, note, 692.
Catelectrotonus, 424, Fig. 161.
Catheter, lung, of Ludwig, 341, Fig. 133.
Cathode, increase of excitability by, 425
  resistance to impulse caused by, 426.
  stimulating effect of, 59, 424.
Cell, animal, like young plant cell, 21.
  as elementary organism, 1, 15.
  assimilation of, induced, 62.
  automatic excitation of, 52.
  chemical stimulation of, 52.
  conductivity in, 62.
  consumption of oxygen by, 27.
  contents, kinds of, 21, Fig. 16; 22.
    morphology of, 20, 21.
  dependence of, upon temperature, 28.
  digestion in, 38.
  effect of external influences on, 50.
  effects of ultra violet rays on, 57.
      of X-rays on, 58.
      of Becquerel rays on, 58.
  electrical stimulation of, 59.
  elimination of decomposition products by, 40.
  form and size of, 16.
  formation of heat in, 46.
  generation of electricity by, 46.
  ingestion of food by, 30.
  mechanical stimulation of, 56.
  membrane, 16.
  motility of, 42.
  osmosis in, 31.
  osmotic pressure in, 31.
  oxidative processes of, 39.
  processes, protoplasmic of, 42; see also *Pseudopodia*.
  production of light by, 45.
  sap of, 21, Fig. 16.
  secretion in, 41.
  stimulation of, by means of heat, 58.
    by means of light, 56.
  vital phenomena of, 22.
Centers, see the various organs and nerves.
Central convolutions, 634, 637, 639, Fig. 289.
  importance of, for vegetative functions, 649, 650.
  motor cortical areas in, 636, 638.
  sensory cortical areas in, 652.
Central nervous system, see various parts of nervous system.
Cereals as food, 139.
Cerebellar peduncles, 593, 612.
Cerebellar tracts in the cord, 593, 595.
  section of, 611.
Cerebellum, 600, 605.
  afferent tracts to, in cord, 593, 611.
  artificial stimulation of, 605.
  bilateral movements from, 640.
  compensation for effects of removal of, 612.
  connections of, 605, 610, Fig. 271.
  distributor of cerebral impulses, 641.
  effects of complete extirpation of, in various lower animals, 605 seq.
    in dog, 606, Fig. 270; 607.
    (unilateral), 612.
  example of regulating influence of, 611.
  field of chief influence of, 609.
  forced movements from, 612.
  lesions of, in man, 607.
  relation of, to labyrinth of ear, 611.
  relaxation of antagonistic muscles from, 636, 640.
Cerebral cortex, electrical stimulation of, 601, 631, 632, 633.
  histological structure of, 634, Fig. 284.
  influence of, on vegetative functions, 599, 649.
  mechanical stimulation of, 633.
  motor areas in, 632.
  proofs that stimulation of, is possible, 633.
  sensory areas in, 650.
Cerebral functions, moral significance of, 672.
Cerebral hemispheres, coöperation of, 641.
Cerebral localization, in brain of apes, 637, 638, Fig. 288.
  in brain of man, 639.
  in brain of monkey, 635, Figs. 285, 286; 636, 637, Fig. 287.
  phrenology compared with, 631.
Cerebrosides, 79.
Cerebro-spinal fluid, 678.
Cerebrum, commissures of, 641.
  compensating of loss of semicircular canals by, 478.
  definition of, 601.
  effects of removal of, from birds, 622, 623.
    from bony fish, 619.
    from dog (Goltz's), 625.
    from dog shark, 619, 620.
    from frog, 620.
    from lizard, 621.
    from rabbit, 624.

Cerebrum, effects of removal of, from turtle, 621.
  myelogenetic areas of Flechsig of, 667.
  physiology of, 629.
  psycho-physical functions of, 658.
  summary of effects of removal of, 627.
  vegetative functions of, 649.
  wanting in human monster, 627.
Cervical sympathetic, see *Sympathetic nerves.*
  as pupilo-dilator nerve, 528.
  as secretory nerve, 258.
  as vasodilator nerve, 235.
Chemotaxis, 53, 54, Fig. 31; 697.
Chemotropic influence, 689.
Chest tones, 505.
Cheyne-Stokes respiration, 333.
Chief cells of gastric glands, 266.
Child, growth of, 707.
  heat regulation in, 409.
  weight of, at birth, 706, 707.
Childhood, period of, 706.
Children, metabolism in, 118, 119.
  nutrition of, 143, 144.
Chlorophyll, 21, 22.
  function of, 23.
  movements of, in *Lemna*, 42, Fig. 25.
Cholagogic substances, 273.
Cholera spirilla, survival of, at low temperatures, 29.
Cholesterin, 80, 254.
  percentage composition of, 82.
Choleic acid, 253.
Cholic acid, 253.
Cholin, 254.
Chondroitin-sulphuric acid, 77.
Chondro-mucoid, 82.
Chondro-proteids, 77.
Chorda tympani as secretory nerve, 257.
  as vasodilator nerve, 235.
Chordæ tendineæ, 166.
Choroid coat, 527.
Chromatic aberration, 526, Fig. 221.
Chromatin, 695.
Chromophyll, 24.
Chronoscope, 673.
Chronotropic effect of vagus excitation, 189.
Cilia, 43, 44.
  mechanism of action of, 44.
Ciliary movements, effects of salts on, 25.
Ciliary muscle, 532, Fig. 227.
Ciliated epithelium of air passages, 323.
  of oviduct, 696.
Circulating proteid, 134.
Circulation, see *Blood.*
  course of, 161, 162, Fig. 50.
  effect of suction of thorax on, 176.
  greater or systemic, 162.
  influence of adrenal bodies on, 365.
  influence of pituitary body on, 367.
Circulation, lesser or pulmonary, 227.
  mechanics of, 200, Fig. 74.
  significance of, for heat regulation, 407.
Circulation of organic elements in nature, 67.
Circulation of protoplasm in plant cells, 42.
Circulatory system, function of, 30.
Chyle, 304, 305.
Chyle vessels, innervation of, 349.
Chyme, 285, 291.
Chymosin, 250.
Clarke's column, 562, Fig. 254; 563.
Cleavage, hydrolytic, 70, 297.
Climacteric, 358, 696, 697.
Closing contraction, 420, 423.
Clostridium Pasteurianum, 23.
Clothing, natural and artificial, use of, 405, 406.
Clotting, see *Coagulation of blood.*
Coagulation of blood, 154, 157.
  importance of, 159.
  why not in blood vessels? 159.
Coagulation of milk, 250.
  of proteid, 75.
  of protoplasm, 29.
Cocaine, effect of, on sense of taste, 485.
  on membranous labyrinth, 476.
Cochlea, 473.
Cochlear nerve, course of, 653, 655.
Cock, castration of, 357, 367, note.
Cold-blooded animals, 46, 442.
  reaction of, to external temperature, 114.
Cold, influence of, on metabolism of warm-blooded animals, 114, 115, 401.
  of simple organisms, 29.
  sensations of, 458.
Cold nerves, 408.
  end-organs of, 468.
Cold sense, 459; 460, Fig. 183.
Cold spots or points on skin, 458, 459, Fig. 182; 461.
Collagen, 78.
  percentage composition of, 82.
Collateral fibers in spinal cord, 563; Fig. 255; 592.
Collateral ganglia, 687.
Color, theories of, 544, 546.
  induction, successive, 542, Fig. 236.
  mixture, 542.
  reactions of proteid, 72.
  sensations, 541.
  system, dichromatic, 546.
    trichromatic, 545.
  tone, 541, 543.
Color blindness, 546, 547.
Colors, complementary, 543.
Colostrum, 704.
Column cells in spinal cord, 563, Fig. 255.
Columns of the spinal cord, 562, Fig. 254; 589, Fig. 261; 591, Fig. 264; 592, Fig. 265; 593.

Combination tones, 501.
Combustion, 26, 27.
  as source of animal heat, 402.
  heat of, 92.
    of foodstuffs, 92.
    of fæces, 93.
    of urine, 93.
Commissures between cerebral hemispheres, 641; see also *Corpus callosum.*
Compensation in ataxia, 473.
  after extirpation of labyrinths, 478.
  after lesions in cerebellum, 612.
Compensatory pause, 183, Fig. 65.
Complemental air, 320.
Complementary colors, 543.
Concomitant respiratory movements, 321.
Conducting pathways, from motor cortical areas, 647.
  in spinal cord, afferent, 592, Fig. 265; 593, 595, 596.
    efferent, 594, Fig. 266; 595.
    methods of determining, 589.
  to auditory area, 614.
  to visual area, 656, Fig. 295; 657.
Conduction, isolation of, in nerves, 41
  of excitation, 411.
  radiation of heat and, 403.
Conductivity, a general property of protoplasm, 62.
  in both directions in nerves, 410.
  not same as excitability, 411.
  resistance to, in nerves, 425, 426.
Conjugated proteids, 75.
Conjugation of male and female elements, 691.
Consciousness, simplest state of, 451, note.
Conservation of energy, 2, 93.
Consonant intervals, 490.
Consonants, 507.
Constant current, 60.
  alterations of excitability produced by, 424.
  stimulating effects of, 423.
Constituents, chemical, of the body, 68.
  inorganic, of animals, 25.
    of plants, 24.
Contractile cells embracing capillaries, 220, Fig. 89.
Contractile vacuoles, 22.
Contraction, auxotonic, 435.
  clonic, 633, 642.
  isometric, 414; 438, Fig. 176.
  isotonic, 415, 435; 436, Fig. 173; 438, Fig. 176; 442, Fig. 178.
  musical tone of, 434.
  opening and closing, 420, 423.
  of pseudopodia, 43.
  Pflüger's law of, 423.
  secondary, 433.
  simple, of cross-striated muscle, 415, Fig. 154.
Contraction, simple, of smooth muscle, 448.
  simple projectile, 436, Fig. 173.
  summated, of cross-striated muscle, 415, 429.
    of smooth muscle, 448.
  tetanic, 429, Fig. 166; 430, Fig. 167.
  veratrin, 437, Fig. 175.
  voluntary, 430.
  tonic, of vascular wall, 238.
    of smooth muscle, 448.
Contractions, fibrillary, of heart, 181.
Contracture after destruction of motor cortex, 646.
  after destruction of cerebellum, 606.
Contrast, simultaneous, in vision, 547.
  explanation of, 548, 549.
Convergence of the eyes, 534, 556.
  accommodation and, 534, 557.
  assymmetrical, 552.
  center of, 535, Fig. 230; 616.
Convolutions of cerebrum, see under individual names.
Cooking, importance of, 110, 242.
Coördination of movements, 473.
  determination of, reflexly, 587.
  in acerebral rigidity, 617.
  loss of, by destruction of internal ear, 478.
    by lesions of cerebellum, 607, 608.
    by loss of motor sensations, 472.
Copper ferrocyanide as semipermeable membrane, 31.
Copulation, 691, 693.
Cornea, form of, 522.
  radius of curvature of, 510, 512.
  refractive index of, 509.
  refractive power of, 513.
Corona radiata, 647.
Coronary arteries, 180.
Coronary veins, 181.
Corpora geniculata, 600, 614, 617, 655, 657
Corpora quadrigemina, 600, 613.
  frontal section of, 615, Fig. 272.
  relation of, to auditory impressions, 614.
    to eye movements, 613.
Corpora striata, 600.
  as heat center, 408.
Corpus callosum, 641.
  section of, 641, 660.
  stimulation of, 641.
Corpus geniculatum external, 617, 657.
Corpus geniculatum internal, 614, 655.
Corpus luteum, 696.
Corpuscles, red, 148; see also *Blood corpuscles.*
  white, 153; see also *Leucocytes.*
Correspondence of the retinæ, 555.
Corti, organ of, 499, 500, Fig. 199.
  pillars of, 499, 500, Fig. 199.
Cortical areas, see *Motor* and *Sensory cortical areas.*

Cortical areas for vegetative functions, 649, 650.
Cortical epilepsy, 632, 641, 642, Fig. 291; 652.
  progress of, 642.
  spread of, through subcortical centers, 643.
Cortical lesions, see *Lesions*.
Cortico-spinal tract in the cord, 593.
Cosmic influences on the body, 61.
Coughing, 321.
Cowper's glands, 691.
Crab, green, osmotic relations of blood of, 34.
  neurofibrils in, 560.
  reflex movements of, 585.
Cramp fish, 49.
Cramplike contractions in cortical epilepsy, 641, 642.
Cranial nerves, 680.
  crossing of motor fibers of, 647.
Crawfish, osmotic relations of blood of, 34.
  nerve fibrils in, 560.
Creatin, 155, 264, 413, 434.
Creatinin, 264, 382, 383, 434.
Cretinous child, 360, Fig. 138.
Crico-arytenoid muscle, lateral, action of, 503, Fig. 201.
  posterior, action of, 503, Fig. 200.
Cricoid cartilage, 502.
Crista acustica, 474.
Crossing of nerve fibers in the brain, 647, 592.
  in the optic chiasm, 657.
  in the spinal cord, 592, 593, 596, 597.
Crystalline lens, distance of, from cornea, 510.
  radius of curvature of, 510, 512.
  refractive index of, 509.
  relation of, to accommodation, 531, Fig. 225; 532 seq.
Crura cerebri, 600, 613, 614.
Ctenolabrus, egg of, in absence of oxygen, 26.
Cubic enlargement of aorta of rabbit, 201, Fig. 75.
  of vena cava of cat, 223, Fig. 92.
Cucumaria, 56.
Curare as lymph producer, 351.
Curare in artificial respiration, 5.
Current clock, 209, Fig. 81.
Currents, electrical; see also under individual names.
  action, 48.
  constant, 59.
  demarcation, 47, 48.
  frog, 47.
  in plants, 49.
  induction, fatal strength of, 61.
  skin, 49.
Curves, central nervous system:
    asphyxiation, resistance of various centers to, 573, Fig. 257.
    cortical epilepsy, course of, 642, Fig. 291.
Curves, central nervous system:
  latent period of muscular contractions induced from cortex underlying white matter, 633, Fig. 283.
  preliminary reflex movements of frog's leg, 571, Fig. 256.
Circulation:
  action current of heart, 13, Fig. 13; 179, Fig. 63; 180, Fig. 64.
  apex beat, 173, Fig. 60; 175, Fig. 62.
  blood pressure:
    depressor, 194, Fig. 70.
    in aorta, 170, Fig. 57; 171, Fig. 58.
    in auricle, 169, Fig. 56; 173, Fig. 60.
    in ventricles, 169, Fig. 56; 170, Fig. 57; 171, Fig. 58; 173, Fig. 60.
    reflex fall, 237, Fig. 98.
    reflex rise, 236, Fig. 97.
    respiratory variations, 229, Fig. 95; 230, Fig. 96.
    vagus stimulation, 205, Fig. 77; 206, Fig. 78; 207, Fig. 79.
  cubic enlargement of aorta, 201, Fig. 75.
    of veins, 223, Fig. 92.
  influence of temperature on, 184, Fig. 66.
  isolated cat's heart, direct stimulation, 183, Fig. 65.
  plethysmographic curve, 212, Fig. 84.
  pulse curve, 12, Fig. 11; 216, Fig. 88.
  pulse rate, 192, Fig. 68; 197, Fig. 71.
  vagus and accelerator compared, 192, Fig. 68.
  velocity curve, 210, Fig. 82.
Digestion:
  digestive action of gastric juice, 265, Fig. 104.
  discharge of bile into intestine, 275, Fig. 110.
  enzymes of pancreatic juice, 271, Fig. 108.
  secretion of gastric juice, 265, Fig. 103.
  secretion of pancreatic juice, 270, Figs. 106, 107.
Growth:
  in length and weight, in boys and girls, 709, Fig. 304.
  variations in length of adult body, 710, Fig 305.
Metabolism:
  excretion of nitrogen in 2-hr. periods, 102, Fig. 44.
  excretion of urea in a fasting dog, 101, Fig. 43.
Muscle and nerve:
  alterations of excitability, 424, Fig. 161; 425, Fig. 162.
  elasticity, 412, Fig. 150; 413, Fig. 152.
  entrance of current through skin to nerve, 428, Fig. 165.
  ergogram, 444, Fig. 180; 445, Fig. 181.

Curves, Muscle and nerve:
    fatigue, 441, Fig. 177; 442, Fig. 178.
    isometric contractions, 438, Fig. 176.
    isotonic contractions, 436, Fig. 173; 438, Fig. 176; 442, Fig. 178.
    projectile motion, 436, Fig. 173; 436, Fig. 174.
    rate of conductivity, 417, Fig. 155.
    simple muscle curve, 7, Fig. 2; 415, Fig. 154.
    stimulation by make and break induction shocks, 426, Fig. 163.
    strength of stimuli and height of contraction, 435, Fig. 172.
    tetanus, 429, Fig. 166; 430, Fig. 167.
    veratrinized muscle, 437, Fig. 175.
  Reproduction:
    curves of intra-uterine pressure in labor, 698, Fig. 302; 699, Fig. 303.
  Respiration:
    absorption of CO_2 by hæmoglobin, 339, Fig. 132.
    absorption of O_2 by blood, 337, Fig. 131.
    elimination of CO_2, 343, Fig. 134; 344, Fig. 135; 345, Fig. 136.
    number of respiratory movements, 319, Fig. 127.
    pneumorgraphic curve of man, 313, Fig. 121.
    respirations influenced by vagus, 328, Fig. 129.
    respiratory curve of rabbit, 314, Fig. 123; 328, Fig. 129.
  Special senses:
    excitation of different components of visual organ by light rays of different wave lengths, 544, Fig. 237; 545, Fig. 238.
    excitation of retina as function of time exposed, 540, Fig. 235.
  Temperature of body:
    daily variations in, 399, Fig. 147.
    post mortal fall of, 401, Fig. 149.
Cutaneous nerves, reflex action of, on respiration, 331.
Cutaneous sensations, 458; see also under *Sensations*.
  tracts for, in the cord, 597.
Cysteïn, 373.
Cystin, 70, 249.
Cytolytic action of blood, 156.
Cytosin, 77.

Dalton's law, for absorption of gases, 334.
Death, 66.
Decidua menstrualis, 697.
Decomposition of carbohydrates, 374.
  of fat, 376.
  of proteids, 369.
Decomposition products, elimination of, by elementary organism, 40.
  in blood, 155.
  influence of, on organs, 356.
  stimulating action of, 52.
Defecation, 298, 299.
Degeneration, of peripheral tissues, 568.
  secondary, in nerve cells, 567, 568.
    in spinal cord, 590, Fig. 262.
  Wallerian, 567.
Deglutition, 279.
  muscles of, 281.
  reflex nature of, 280.
  sounds of, 282.
Delomorphous secreting cells, 267.
Demarcation current, 47, Fig. 29; 48.
  in spinal cord, 588.
Dendrites of nerve cell, 559.
Density of current, 420.
Depressor nerve of heart, 193.
Depth, perception of, in vision, 556.
Deuteroalbumoses, 249.
Development, see *Growth*.
  of myelin substance in brain, 667.
Dextrins, formation of, in digestion, 246.
  properties of, 82.
Dextrose, as product of digestion, 246, 251.
  as source of glycogen, 127.
  from alanin, 373.
  from lactic acid, 374, note.
  from leucin, 374.
  in urine, 383; see also *Diabetes*.
  properties of, 80.
Diabetes mellitus, 127, 375.
Diabetes, pancreatic, 127, 128, 362, 375.
  phloridzin, 127, 374, 375.
  puncture, 375.
Diamino acids, 70.
Diamino-caproic acid, 70.
Diamino-valerianic acid, 70, 72, 370.
Diaphragm, movements of, in respiration, 316.
  paralysis of, 324.
Diaphragmatic type of respiration, 318.
Diastatic enzyme, definition of, 243.
  in bile, 254.
  in intestinal juice, 255.
  in pancreatic juice, 251.
  in saliva, 246.
  in sweat, 395.
  preserved in stomach, 291.
Diastole, definition of, 162.
  suction of heart in, 177, 225.
  time relations of, 175, Fig. 62; 176.
Dibasic monamino acids, 70.
Dichromatic color system, 546.
Dichrotic elevation, 175.
  on cardiogram, 173, Fig. 60; 175, Fig. 62.
  on sphygmogram, 216, Fig. 88.

Diencephalon, 600, 601, 617; see also *'Tween-brain.*
Diet, see *Nutrition* and *Nutritive requirements.*
  animal and vegetable, 145.
  construction of, 145.
  digestibility of, in stomach, 293.
  importance of variation in, 134.
  mixed, utilization of, 139.
  natural, of man, 146.
Difference tones, 501.
Difflugiæ, motility of, 45.
Diffusion, absorption and, 353; see also *Osmosis.*
  of odors, 486, 487.
  relation of, to excretion, 41.
Digestibility of food in stomach, 293.
Digestion, artificial, 244, 248.
  definition of, 38.
  Bacterial, in intestine, 297.
  in different divisions of alimentary canal, 290 seq.
  in intestine, 294 seq.
  in large intestine, 298.
  in mouth, 290.
  in stomach, 291.
  in unicellular organisms, 38.
  intracellular and extracellular, 38.
  metabolism and work of, 108.
Digestive enzymes, 243; see also *Enzymes.*
Digestive fluids, 242 seq.; see also under individual names.
  methods of study of, 243.
  secretion of, 256 seq.
Digestive glands, 256 seq.; see also individual glands.
  conditions for secretion in, 256.
  electric phenomena of, 48, 49, 257.
  extracts of, 243.
  fistulæ of, 243.
  heat production in, 257.
  morphological changes in, 260, Fig. 100; 261, Fig. 101; 262, Fig. 102; 272, Fig. 109; 277, Fig. 111.
  specific excitants of, 264, 271, 275.
Digestive products, effects of injection of, into blood, 250.
Digestive system, function of, 30.
Dihexosamin, 249.
Dilator center of pupil, 529.
Dilator nerves of pupil, 528.
Diopter, definition of, 513, note.
Dioxy-phenyl-acetic acid, 384.
Dioxy-pyrimidin, 76.
Direct vision, 514.
Direction, lines of, in vision, 518.
Directive influences on movements of organisms, 59, note.
Disaccharides, properties of, 81.
  percentage composition of, 82.
Discrimination time, 676.
Discus proligerus, 695.
Dispersion circle, 517.
Dissimilation equivalent to oxidation, 27.
Dissimilation, necessity of, to growth, 26.
Dissimilation source of kinetic energy, 26.
Dissociation, electrolytic, 32.
Distances, estimation of, with eye, 554.
Distribution of blood in body, 239.
Diuresis, 390.
Diuretic substances, 273, 389, 390.
Dizziness in the deaf and dumb, 481.
Dog, extirpation of cerebrum in, 625.
  extirpation of spinal cord in, 581, 582, 587.
Dorsolateral cerebellar tract, 593.
Double refraction of contractile protoplasm, 20.
Double vision, 555.
Dromotropic effect of vagus, 189.
Dry rigor, 20.
Dry substance, determination of, in food, 84.
  utilization of, in body, 139.
Dulcite, 80.
Duodenum, influence of, on evacuation of stomach, 285.
  secretion of pancreatic juice and, 270.
Dyspnœa, 332.

Ear, analysis of sound in, 493, 498.
  auditory ossicles of, 495.
  beats, how explained, 501.
  cochlea of, 498.
  combination tones in, 501.
  Eustachian tube of, 497, 498.
  excitation of auditory nerve in, 498.
  external, 494.
    movements of, on stimulation of brain, 658.
    vasodilator nerves of, 235.
  intrinsic muscles of, 497.
  middle, 494, 495, Figs. 196, 197.
  organ of Corti in, 499, 500, Fig. 199.
  otolith sacs of, 473, 481.
  resonance theory of hearing in, 498.
    objections to, 501.
  resonators in, 498.
  semicircular canals of, 473.
  transmission of sound in, 493.
  tympanic cavity of, 495, 497.
  tympanic membrane, 494, 495, 496.
Earthworm, phototaxis of, 57.
Echinoderms, galvanotaxis of, 60.
Echinoderms (*Asterina*), geotaxis of, 56.
Eck fistula, 227, 274, 371.
Edestin, 70, 71.
Egg, white of, 245.
Egg albumin, 74, 264.
Eggs, dependence of, on oxygen, 26.
  osmotic phenomena in, 34.
  thigmotactic influence of, 697.
Ejaculation, 693.

Elastic manometer, 9, Fig. 5.
Elastic tubes, flow of liquid in, 199.
  waves in, 212.
Elasticity, coefficient of, in arteries, 201.
  of arterial wall, 200, 201.
  of lungs, 310; 311, Fig. 120; 317.
  of resting muscle, 412, Fig. 150; 413, Fig. 152.
Elasticity apparatus, 412, Fig. 151.
Elastin, 78.
  percentage composition of, 82.
Electric fishes, 48, 50.
Electric phenomena in central nervous system, 570, 588.
  in cutaneous glands, 48.
  in digestive glands, 257.
  in muscles and nerves, 47, 431.
  in plants, 49, 50.
  in resting muscle, 47.
  in retina, 537.
  in skin, 49.
  in starch formation, 49, 50.
Electric signal, 10, Fig. 7.
Electrical stimulation in general, 59, 418.
Electrical stimulation of the cord, 588.
Electrical stimulation of the cerebral cortex, 601, 631, 632, 633.
Electrical stimulation of human nerves, 427.
Electricity, see *Electric currents.*
  action of strong currents of, 61.
  animal, 46.
  generation of, 46.
Electrodes, nonpolarizable, 418, 419, Fig. 157.
Electrolysis in nerves, 434.
Electrolytes, relation of, to osmotic pressure, 32.
Electrometer, capillary, 13, Fig. 12.
Electrotonic currents, 433, Fig. 171.
Electrotonus, see *Anelectrotonus* and *Catelectrotonus.*
Elements, chemical, behavior of, in metabolism, 131 seq.
  necessary for animal body, 25, 26.
Elements of speech, 506.
Emmetropic eye, 519.
Emotions, rationalized, moral power of, 672.
  summoning influence of, on memory, 671.
Emulsion in intestine, 295, 296.
Encephalon, 600; see also *Brain.*
End products, of proteid digestion, 249.
End products, nitrogen equilibrium on, 124.
Endbrain, 600, 601; see also *Cerebrum.*
Endolymph, in cochlea, 497, 498.
  movements of, in semicircular canals, 479, 480.
Energy, conservation of, 2.
  in animal body, 93, 94.
  kinetic, 26.
  liberated, greater than energy of stimulus, 51.
Energy, potential, measure of, in substance, 26.
    of foodstuffs, 92.
    stored in processes of assimilation, 26.
    transformation of, into external work, 113.
    utilization of, in diet, 139.
  production of, in cells, 26.
  requirements of, of an adult man, 140.
    of an adult woman, 143.
    of children, 144.
  source of, in muscular work, 112, 113.
  total output of, in muscle, 439.
Entoptic phenomena, 521.
Enterokinase, 252, 255.
Enucleated cells, 18.
Enzymes, 38, 356.
  amylolytic, 243, 251.
  in bile, 254.
  in blood, 155.
  in liver cells, 375.
  in pancreatic juice, 251.
  lipolytic, 243, 253.
  measure of activity of, 245.
  precursors of, 244.
  preotolytic, 243, 252.
  properties of, 38.
  reversible processes of, 39.
Epididymus, 693.
Epiglottis in swallowing, 281, Fig. 112; 282.
Epiglottis laryngoscopic picture of, 504, Fig. 202.
Epilepsy, cortical, 632, 641, 642, Fig. 291; 652.
Epilepsy in myxœdema, 360.
Epithalamus, 600.
Equilibrium, loss of, after removal of cerebellum, 606.
  nitrogenous, 91, 100, 103, 120, 121, 122.
  of substance in body, 137.
Equimolecular solutions, 32, 33.
Erection, 588, 693.
  center of, 694.
Erepsin, 255, 305.
Ergograph, 443, 444, Fig. 179.
Ergographic record, 444, Fig. 180; 445, Fig. 181.
Erlanger's apparatus, for determination of blood pressure in man, 203, Fig. 76.
Erucic acid, 130.
Erythrodextrin, 246.
Ethereal sulphates, 373, 379.
Eudendrium, 64.
Euglobulin, 154.
Eustachian tube, 498.
Evacuation of large intestine, 299.
  of stomach, 285.
Excitability, alterations of, 52, 425.
  by extraction of water, 53.
  influence of heat on, 58.
Excitants, specific, in secretion, 264, 271, 275.

Excitation, see *Stimulation.*
  accompanied by heat and electricity, 51.
  automatic, 52, 356, 570, 580.
  of muscle and nerve, 414.
  polar law of, 424, 426.
  propagation of, through the heart, 187.
  rate of transmission of, see *Transmission of stimulus.*
Excrements, see *Fæces.*
Excreta, apportionment of chemical elements to, 89.
  determination of, in metabolism experiments, 84; see also various excretory organs.
Excretion, definition of, 40.
  by kidney, 384.
  by lungs, 346.
  by skin, 394.
  in unicellular organisms, 40.
  of carbon dioxide, 89.
  of iron, 308, 309.
  of nitrogen, 89, 90.
  through intestine, 133, 298, 309.
Excretory organs, function of, 31.
Expansion of thorax, 310, 312.
Expansion movements of pseudopodia, 43.
Expiration, see *Respiration* and *Respiratory movements.*
  definition of, 310.
  description of, 317.
  effects of, on arterial blood pressure, 230.
  muscles of, 317.
  pressure changes in air passages in, 321, 322.
    in thorax in, 310, 312.
Expired air, composition of, 342.
  poisonous constituents in, 344.
Expulsion period in parturition, 698.
Extension, curve of, in resting muscle, 412, Fig. 150; 413, Fig. 152.
External auditory meatus, 494, Fig. 196.
Extractives, effect of, on gastric glands, 264.
  food value of, 109.
Extremities, vasoconstrictor nerves of, 232.
  vasodilator nerves of, 235.
Eye, accommodation in, 529 seq.
  after-images of, negative, 539.
    positive, 538.
  binocular field of vision of, 551, 552, Fig. 242.
  blind spot of, 516, Fig. 212.
  cardinal points of, 512, 513, Fig. 210.
  changes produced in retina of, by action of light, 537, Fig. 231; 538, Fig. 232.
  choroid coat of, 527.
  convergence of visual axes of, 534, 556, 557, Fig. 230.
    center for, 535.
  dichromatic, 546.
  dispersion circles in, 517.
  emmetropic, 519, Fig. 215.
Eye, excitation of retina of, 536.
  far-point of, 520.
  fatigue and recovery of, 539.
  focal distances of, 512.
  fovea centralis of, 514, 517, 541.
  hypermetropia of, 519, Fig. 215; 520.
  images, formation of, on the retina of, 513, 556, Fig. 248.
  iris of, 527.
  light-perceiving layer of retina of, 514.
  muscular strabism of, 555.
  myopia of, 519, Fig. 215.
  near-point of, 529.
  optical constants of, 508.
  optical defects of, 520.
    angle between line of vision and visual axis, 525.
    astigmatism, 522, 524, Fig. 219.
    chromatic aberration, 526, Fig. 221.
    entoptic phenomena, 521, Fig. 216; 522, Fig. 217.
    form of refracting surfaces in, 522.
    spherical aberration, 522, 523.
  ora serrata of, 514.
  perception of depth by, 556.
  primary position of, 549.
  pupil of, constriction of, 528.
      center for, 529.
    dilatation of, 528.
      center for, 529.
  reduced, 512.
  refracting media of, 508.
  refraction in, 510, Fig. 207.
  rotation center of, 549.
  schematic, 511, 513, Fig. 210.
  sensations of color in, 541.
    complementary colors, 543.
      successive color induction, 542.
      theories of color vision, 544, 546.
  simultaneous contrast in vision in, 547.
    explanation of, 548, 549.
  static refraction of, 519, Fig. 215.
  stereoscopic vision of, 558.
  trichromatic, 545.
  ultra-red rays, effect of, on, 536.
  ultra-violet rays, effect of, on, 53.
  visible rays of spectrum in, 536.
  visual angle and limits of vision in, 517.
Eye as an optical instrument, 508.
Eye movements, 549.
  induction of, by stimulation of cerebral cortex, 640, 658.
  limits of, 551, Fig. 241.
  relation of corpora quadrigemina to, 613.
  significance of, for projection of visual impressions, 552.
  synergic, 616.
Eye muscles, 549.
  action of, 549, 550, Fig. 240.

Eye muscles, axes of rotation in, 550, Fig. 240.
  centers for, 614, 615, Fig. 273.
  innervation of, 680.
Eyes, single vision with two, 555.

Face mask for respiration experiments, 85, Fig. 39; 105.
Face muscles, contraction of, by stimulation of cortex, 640.
Facial nerve, 680.
  as nerve of expression, 680.
  as nerve of taste, 484, Fig. 191.
  as secretory nerve of salivary gland, 257.
Fæces, demarcation of, 85.
  formation of, 298.
  heat of combustion of, 93.
  in fasting, 96.
  metabolic significance of, 90.
  N:C in, 90.
Fallopian tubes, 696.
Falsetto voice, 505.
Far-point, 520.
Fasting, 95.
  cause of death by, 98.
  fæces formed in, 96.
  in animals of different size, 117.
  influence of, on different organs, 97, 98.
    on fatigue, 445.
  metabolism in, 95, 96.
  of elementary organisms, 28.
  physiological condition in, 95.
Fat, absorption of, 304.
  cells, 21.
  chemical nature of, 79.
  cleavage theory of digestion of, 296.
  determination of, in food, 84.
  digestion of, by pancreatic juice, 253.
    in intestine, 295.
    in stomach, 250.
  droplets in various cells, 22.
  dynamic value of, 93.
  emulsion theory of digestion of, 295.
  final decomposition of, 376.
  form of, in milk, 701.
  formation of, in mammary glands, 705.
  from fatty acids, 130.
  in blood, 155.
  in mucins, 74.
  in muscle, 413.
  influence of, on gastric digestion, 285, 293.
    on metabolism, 104.
  metabolism of, in fasting, 97, 104.
    in muscular work, 113.
  percentage composition of, 82.
  physiological heat value of, 93.
  proteid sparer, as a, 121.
  relation of, to glycogen, 128.
    to pancreatic secretion, 270.
    to proteid retention, 121.
Fat, resynthesis of, 304.
  sources of, in body, 129, 130.
  storage of, in body, 129.
  subcutaneous, as protection against heat loss, 405.
  transportation of, in body, 376.
  utilization of, 138.
Fatigue, 65.
  effect of, on power of localization, 464.
  influence of mental work on, 446.
  local, 442.
  of brain, 676.
  of ear, 499.
  of muscles, 441.
    human, 443.
  of nerves, 442.
    human, 443.
  of olfactory organ, 488.
  of visual organ, 539.
  rate of stimulation and, 446.
  record of, with ergograph, 444, Fig. 180; 445, Fig. 181.
Fatty acids, food value of, 109.
  production of, by digestion, 295.
  solubility of, in bile, 254, 296.
Fatty degeneration, 129.
Fatty infiltration, 129.
Fat-splitting enzymes, 250, 253; see also *Steapsin.*
Feathers as protection against heat loss, 405.
Fechner's psycho-physical law, 457, note.
Feeding, fictitious, 263.
Feeling, general state of, 452.
Feeling of effort in motor sensation, 470.
Feelings, summoning power of, on memory, 671.
Fellic acid, 253.
Female sexual organs, 695; see also *Sexual organs.*
Fenestra ovalis, 496.
Fenestra rotunda, 497.
Ferment action, 40.
Fermentation, alcoholic, 28, 40, 80.
Ferments, organized, 40; see also *Enzymes.*
Fertilization, 691, 697.
Fibrillary contractions of heart, 181.
Fibrin, 147.
  formation of, 157, 158.
Fibrin ferment, 158.
Fibrinogen, 154, 157.
  cleavage of, 158.
Fibrino-globulin, 159.
Fillet, 592.
  lateral, 614, 655.
Filtration, theory of, in urine formation, 387.
  in lymph formation, 349.
Fimbria ovarica, 696.
Fish, effect of low temperature on, 29.
  electric, 48, 50.

Fish, extirpation of cerebrum in, 619.
  geotaxis of, 56.
Fissure, calcarine, 639, Fig. 290; 659.
  cruciate, 624, Fig. 280.
  of Rolando, 639, Fig. 289.
  of Sylvius, 624, Fig. 280; 639, Fig. 289.
Fistula, biliary, 243, 298.
  Eck's, 227, 274, 371.
  fundus, 264.
  gastric, 243, 246.
  intestinal, 243, 295.
  œsophageal, 263.
  pancreatic, 243, 251.
  pyloric, 267.
Flagella, definition of, 43, 44.
  vibrations of, independent of NaCl, 25.
Flagellata, 44.
Flavors, 133.
Flechsig's tract or bundle in the cord, 591, Fig. 264; 593.
Flow of blood in arteries, 200 seq., 218.
  in capillaries, 219.
  in veins, 223.
Flow of liquid in elastic tubes, 199.
  in rigid tubes, 198, Fig. 72; 199, Fig. 93.
Fluids, absorption of, gases by, 334.
Fluttering of heart, 187.
Focal distances of the eye, 512.
Focal lines, 523, 524, Fig. 219.
Focal points in eye, 512, 513, Fig. 210.
  in optical system, 510, Fig. 207; 511, Fig. 208.
Folin's theory of proteid metabolism, 137.
Follicle, graafian, 695.
  primary, 695.
Food, construction of diet from different articles of, 145.
  definition of, 137.
  influence of, on metabolism, 98.
Food requirements, see *Nutrition.*
  of grown man, 140.
  of grown woman, 143.
  of infants, 144.
  of youths, 143.
Foodstuffs, see *Metabolism*, *Nutrition diet*, and individual foodstuffs.
  decomposition of, 369.
  definition of, 83.
  inorganic, 83, 131.
    effect of deprivation of, 131.
  organic, 83.
  plastic, 111.
  potential energy of, 92.
  replace one another, 93.
  respiratory, 111.
Foraminifera, 41.
Forced movements and positions, 612.
Forebrain, 600.
Fovea centralis, 514, 517, 541.
Freezing point, lowering of, 32.
Frittillaria imperialis, 21, Fig. 16.
Frog, extirpation of cerebrum in, 620.
  behavior of, in absence of O_2, 27.
  galvanotaxis of, 60.
  geotaxis of, 56.
  osmotic relations in, 34.
Frog current, 47.
Frontal association centers, 668, 669.
Frontal convolutions, 631, 637, 638, 639, Figs. 289, 290; 664.
Frontal lobes, extirpation of, 668.
Frontana leucas, 41, Fig. 24.
Fructose, 80; see also *Levulose.*
Fruit sugar, 80; see also *Levulose.*
Fruits as exclusive food of man, 146.
Fundamental colors, 544, 547.
Fundamental tone, 491, 492, Fig. 194.
Fundic glands, 266.
Fundulus, egg of, 25, 34.
Fundus fistula, 264.

Galactose, 80, 81, 251.
Gall bladder, 275.
Galvani's discovery, 46.
Galvanotaxis, 60.
Galvanotropism, 64, 65.
Ganglia, basal, of brain, 632.
  collateral, 687.
  lateral, 687.
  peripheral, 583; 584, Figs. 258, 259.
  spinal, chief purpose of, 584.
  sympathetic, reflexes through, 583.
    table of connections of, 688.
Ganglion, inferior mesenteric, 392, Fig. 145; 393, 688.
  stellate, 687, 688.
  superior cervical, 689.
  superior mesenteric, 392, Fig. 145; 393.
Ganglion cells, degeneration of, 585.
  in heart, 186, 190.
  in intestinal wall, 288; see also *Auerbach's plexus* and *Meissner's plexus.*
  in stomach wall, 284, Fig. 114.
  in ureter wall, 391.
  peripheral, functions of, 583.
    reflexes through, 584, Fig. 259.
Gas pump, 334, Fig. 130.
Gases, absorption of, in liquids, 334.
  exchange of, between alveolar air and blood, 340.
    between blood and lymph, 342.
  in blood, 333, 339.
  in intestine, 295.
  pressure of, in alveoli, 341.
  tension of, in tissues, 342.
Gastric glands, 266.
  morphological changes in, 268.
  nerves of, 263.

Gastric juice, 246.
  acid of, 247.
  antiseptic properties of, 292.
  hourly course of digestive action of, 265, Figs. 103, 104.
  pepsin in, 248, 268.
  rennin in, 250, 267.
Gastric mucus, 266.
Gastric steapsin, 250.
Gelatin, 78.
  composition of, 75, 82.
  digestion of, 247, 252.
  food value of, 109.
  products of digestion of, 75, 78.
Gelatin peptones, 78.
Gelatin-forming substances, 247.
  digestion of, 247, 252, 291, 294.
  food value of, 109.
Generation, organs of, see *Sexual organs.*
    vasomotor nerves of, 233, 235.
  spontaneous, 16.
Geotaxis, 56.
Geotropism, 64.
Germinal spot, 695.
Germinal vesicle, 695.
Gestation, period of, 698.
Giant cells of algæ, 16.
  of bone-marrow, 16.
Girlhood, age of, 706.
Girls, food requirements of, 144.
  growth of, 708, 709.
Glands, albuminous, 245, 261.
  gastric, 266.
  lachrymal, 245.
  mixed, 245.
  mucous, 245, 261.
  of large intestine, 277, Fig. 111.
  of small intestine, 276.
  parotid, 245, 257.
    of cat, 261, Fig. 101.
    of rabbit, 260, Fig. 100.
  preputial, of mouse, 394, Fig. 146.
  salivary, 257 seq.
  sebaceous, 394.
  sublingual, 245, 257, 258.
  submaxillary, 245, 257, 258.
Globin, 75, 152.
Globulins, 74.
  alkaline combination of, in blood, 338.
  of blood, 154.
Glomerulus of kidney, 385.
Glossopharyngeal nerve, 484, 681.
  as nerve of taste, 484, Fig. 191.
  as secretory nerve of salivary glands, 257.
  respiration and, 331.
Glottis, 502.
Glucosamin, 71, 72.
Glucose, 80; see also *Dextrose.*
Glutamic acid, 70, 72, 249.
Glutin-forming substances, 250; see also *Gelatin-forming substances.*
Glyceric acid, 377.
Glycerides, 79.
Glycerin, food value of, 110.
  from cleavage of fat, 295.
  in blood, 155.
Glycerin aldehyde, 373.
Glycerin-phosphoric acid, 78.
Glycocholic acid, 253.
Glycocoll, 70, 72, 253, 370, 378.
Glycogen, 81, 124, 374 seq.
  affected by extirpation of pancreas, 364.
  amount of, stored in body, 125.
  consumption of, in muscular work, 126.
  formation of, from carbohydrates, 126.
    from fats, 128.
    from proteids, 127.
  in liver, 125, 126, Fig. 45.
  in muscle, 413.
  in nature, occurrence of, 81.
  percentage of, in various organs of body, 125.
  transformation of, into sugar, 375.
Glycogenic function of the liver, 375.
Glycol, 377.
Glycolic acid, 377.
Glycosuria alimentary, 127, 363, 374.
Glycuronic acid, 376, 379, 383.
Glyoxylic, 377.
Golgi's method, 559.
Goll's column in the cord, 591, Fig. 264; 592.
Gower's tract or bundle in the cord, 591, Fig. 264; 593.
Graafian follicle, 695.
Grape sugar, 80; see also *Dextrose.*
Graphic method, 6.
Gray, extracellular, of Nissl, 561.
Gray matter of spinal cord, 562, 589.
Gray rami communicantes, 687.
Green blindness, 546.
Gromia oviformis, 35, Fig. 19.
Growth energy, inherent in cells, 63.
Growth of human body, 705 seq.
  by years, 708, 709.
    of males and females, 709, Fig. 304.
  factors determining rate of, 707.
  influence of economic circumstances on, 710.
    of puberty on, 708, 709, 710.
    of season on, 710.
  periods of, 706.
Guanidin rest, 70, 72.
Guanin, 76, 252, 413.
Guanylic acid, 77.
Gudden's method of tracing nerve paths, 568, 591.
Gums, properties of, 82.
Gymnemic acid, 485.
Gyrus angularis, 662, Fig. 296; 663.
Gyrus fornicatus, 639, Fig. 290; 653.

Gyrus marginalis, 634.
Gyrus sigmoides, 266, 632, Fig. 282.
Gyrus supramarginalis, 662, Fig. 296

Hallucinations, visual, 454.
Haploscope, 555.
Haptogen membrane of milk, 701.
Hæmatin, 152.
Hæmatinic acid, 254.
Hæmatogens, 308.
Hæmatoidin, 254.
Hæmatoporphyrin, 152, 383.
Hæmin crystals, 153, Fig. 49.
Hæmochromogen, 75, 152.
Hæmodromograph, 209, Fig. 81.
Hæmoglobin, 150, 151.
  absorption of CO_2 by, 339, Fig. 132.
  absorption of O_2 by, 336.
  absorption spectra of, 151, Figs. 47, 48.
  carbon-dioxide, 152.
  carbon-monoxide, 152.
  nitric-oxide, 152.
  percentage of, in red blood corpuscles 150.
  relation of, to bile pigments, 254.
  union of, with CO_2, 339.
Hæmoglobins, 75.
Hæmopyrrol, 152.
Hair as protection against loss of heat, 405.
Hair cells of organ of Corti, 499, 500, Fig. 199.
Hammer of middle ear, 495, Fig. 197; 496 Fig. 198.
Head, vasomotor nerves of, 232, 235.
Head tones, 505.
Hearing, see *Ear*.
  cortical field for, 653, 654, Fig. 293.
  range of, 490.
  reaction time to, 673, 674.
  sense of, 451, 489.
Heart, action current of, 13, Fig. 13; 179, Fig. 63; 180, Fig. 64.
  anæmia of, 181.
  artificial nourishment of, 25, 182.
  automatism of, 185.
  chambers of, 161; see also under individual names.
  changes in form of, 163, 164.
  changes of pressure in, 168 seq.
  compensatory pause of, 183, Fig. 65.
  contraction of, nature of, 179.
  coronary circulation in, 180.
  cross section through, 163, Fig. 51.
  diastole of, 162, 176.
  electrical stimulation of, 182 seq.
  fibrillary contractions of, 181.
  filling of, in diastole, 176.
  fluttering of, 187.
  influence of thoracic suction on, 176.
  intrinsic ganglia of, 186.
  Krehl's cone of, 163, Fig. 52.
Heart, movements of, 162.
  nutrient medium for, 25, note, 182.
  nutrition of, 180.
  period of ejection of, 171.
  period of rising tension of, 170, 175.
  power of, 177, 178.
  pressure in different chambers of, 169.
  propagation of excitation wave in, 187.
    muscular theory, 186.
    nervous theory, 187.
  pulse volume of, 204.
  reflexes, 193.
  refractory period of, 183, Fig. 65.
  separation of auricles from ventricles in, 185, 189.
  sounds, 167, 168, 175.
  structure of wall of, 162, 163.
  suction of, in diastole, 177.
  systole of, 162.
  tactile sensations in, 194.
  tenacity of life in, 182.
  tetanus of, 184.
  time relations of events in, 170, 171; 173, Fig. 60; 175, Fig. 62; 176.
  valves of, 165.
  variations of electrical potential in, 179, Fig. 63.
  vasomotor nerves of, 233, 235.
  work of, 178.
Heart beat, acceleration of, by inflation of lungs, 195.
  cause of, 185.
  force of, 188.
    influence of blood on, 184, 204.
      of vagus on, 189.
  frequency of, as affected by age, 197.
    by food, 197, Fig. 71.
    by individual peculiarities, 198.
    by muscular exercise, 197.
    by sex, 197.
    by size of body, 197.
    by temperature, 184, Fig. 66; 19
    by vagus nerve, 188.
Heart muscle, contraction of, nature of, 179.
  propagation of excitation wave in, 187.
  properties of, 179.
Heart nerves, 188.
  accelerator, 191, Fig. 67; 688.
  afferent, 193.
  centers for, 195.
  depressor, 193, Fig. 69; 681.
  efferent, 188.
  inhibitory, 188; 191, Fig. 67.
  reflexes through, 193.
Heat, conduction and radiation of, 403.
  formation of, universal in nature, 46.
  influenced of, on elementary organisms, 29.
  production of, in cold-blooded animals, 46.
    in man, 402.

Heat, production of, in plants, 46.
Heat as stimulus, 58.
Heat centers, 408.
Heat loss, from the body by different means, 403.
  protection against, 404.
  regulation of, 407.
Heat nerves, 408.
  end organs of, 468.
Heat production, 46, 402.
  amount of, in human body, 94.
  in glands, 402.
  in muscles, 402, 439.
  in nervous system, 402.
  influenced by amount of food, 407.
    by muscular work, 116.
    by surrounding temperature, 114.
  ratio of, to external work of muscle, 440.
Heat regulation, 407.
  centers for, 408.
  disturbances to, by extirpation of thyroid, 361.
  in the newborn, 409.
Heat sense, 459; see also *Temperature sensations.*
  topographical distribution of, 460, Fig. 183.
  tracts for, in the cord, 597.
Heat spots on the skin, 458; 459, Fig. 182; 461.
Heat units, 26, note.
Heliotropism, 64.
Heller's test for proteid, 69, 384.
Hemiamblyopia, 655, 660.
Hemianopia, 657.
Hemilesion of the cord, 597.
Hemiplegia, 646.
Hemisection of the cord, 595, 596, 640.
Hemispheres of the brain, 600.
Henle's loop, 385, Fig. 144; 386.
Henry's law of absorption of gases, 334.
Hepato-pancreas of isopod, 244, Fig. 99.
Hering's theory of color vision, 544, 546.
Hermann's theory of animal current, 48.
Heteroalbumose, 249.
  food value of, 108.
Hexoses, occurrence of, 80.
Hindbrain, or rhomencephalon, 600, 601.
  secondary, or metencephalon, 600, 601.
Hippuric acid, 155, 378, 383.
Histidin, 72, 255.
Histological methods, 4.
Histons, 77.
Homocentric bundle of light rays, 523, note.
Homoiothermous animals, 46, 398, 404, 442.
Hyaloplasm, 19.
Hydrobilirubin, 254.
Hydrochloric acid, action of, on ptyalin, 246.
  antiseptic properties of, 292.
  influence of, on tryptic digestion, 294.
  of gastric juice, 247.
Hydrochloric acid, where formed, 268.
Hyoglossal muscles, action of, in deglutition, 280, 281.
Hydrolytic cleavage, 70, 243.
Hydrometric pendulum, 210.
Hyperæmia, influence of, on transudation, 349.
Hyperæsthesia, 597.
Hypermetropia, 519; Fig. 215; 520.
Hypertonic solutions, 32.
Hypogastric nerves, 392, Fig. 145; 693, 700.
Hypogastric plexus, 392, Fig. 145, 393, 694, 700.
Hypoglossal nerve, 681.
Hypophysis cerebri, 367; see also *Pituitary body.*
Hypotonic solutions, 32.
Hypoxanthin, 76, 252, 372, 373, 413.

Ideas, definition of, 451, note.
  formation of, 662.
Idiocy, 670.
Images in eye, 513 seq., 556, Fig. 248.
  in optical system, 511, Figs. 208, 209.
Imbecility, 669.
Imbibition, capillary and molecular, 353.
Immunity, 156.
Inanition, state of, 155; see also *Fasting.*
Incidence, angle of, 509, Fig. 206.
Incoördination of movements, 608; see also *Coördination of movements, loss of.*
Incubation, liberation of oxygen in, 27.
Incus of middle ear, 495, Fig. 197.
  articulation of, with malleus, 496, Fig. 198.
Indican, 379.
Indigosulphate of sodium, elimination of, by kidneys, 388.
Indol, 378, 379.
Indol nucleus in proteid, 71.
Indoxyl, 379.
Indoxyl-sulphuric acid, 379.
Induction coil, 419, 420, Fig. 158.
  currents, 426.
  shocks, 422, 423.
  stimulation of muscles and nerves by, 418, 422, Fig. 160.
  unipolar effects of, 426, Fig. 163.
Infundibulum, 600.
Infusoria, chemotaxis of, 55.
  geotaxis of, 56.
  ingestion of food in, by ciliary action, 37.
  osmotic relations in, 34.
Ingesta, determination of, in metabolism, 83.
Ingestion of food by elementary organism, 30, 36, Fig. 21; 37.
Ingestion of foreign bodies by leucocytes, 37.
Inhibition, definition of, 50.
  of auricle, 189.
  of central veins, 189.
  of muscles, antagonistic, 640.

Inhibition of reflexes, 577.
  of ventricle, 189.
Inhibitory centers, 579.
Inhibitory nerves, 564.
  of gastric glands, 263.
  of intestinal glands, 276.
  of intestinal movements, 288, 289, 290.
  of heart, 188 seq.
    centers for, 195.
    course of, 191, Fig. 67; 681.
  of pancreas, 269.
  of stomach musculature, 284.
Inoculation, protective, 29.
Inorganic foodstuffs, 83.
Inorganic substances, see *Mineral substances*.
  absorption of, 139, 307.
  of blood, 154.
  of diet, 139.
  of food, 83.
  of milk, 702.
  of urine, 384.
Inotropic effect of vagus on heart, 189.
Inosinic acid, 413.
Inosit, 413.
Iodin, amount of, in blood of dog, 351.
  as constituent of thyroid gland, 26, 362.
Iodothyrin, 362.
Ions, dissociation of, 32.
  permeability of cells to, 34, 35.
  relation of, to sense of taste, 485.
  stimulating effects of, 53.
Insensible perspiration, 397.
Inspiration, influence of, on arterial blood pressure, 229.
  pressure changes in air passages in, 321.
    in thoracic cavity in, 312.
Inspiratory muscles, 315, 316.
Insula, see *Island of Reil*.
Intercellular bridges, 62, Fig. 36.
Intercostal muscles, 315, 324.
Interference of sound waves, 501.
Intermediary myelogenetic regions of the cortex, 667.
Internal capsule, motor fibers in, 637, Fig. 287; 647, Fig. 292.
Internal secretion, definition of, 356.
  of adrenal bodies, 364.
  of kidneys, 367.
  of ovaries, 358.
  of pancreas, 362.
  of pituitary body, 367.
  of spleen, 368.
  of testes, 357.
  of thyroid, 358.
Interrupter, automatic, of induction coil, 421, Fig. 159; 422, Fig. 160.
Intersystole, 170, Fig. 57; 174.
Intoxication, 30.
In[illegible]al ganglion cells, 186.
Intracardial pressure, 169, Fig. 56.
Intracranial pressure, 678.
Intrathoracic pressure, 310.
  data for, in man, 312.
  demonstration of, 311, Fig. 120.
  methods for determining, 311
Intrauterine pressure, 698, 699.
Intravascular clotting, 159; see also *Coagulation*.
Inversion of disaccharides, 81.
Intestinal epithelium and absorption of fat, 304, Fig. 118.
Intestinal fistulæ, 243, 295.
Intestinal gases, 295.
Intestinal glands, 276.
Intestinal juice, 255.
Intestinal movements, 286, 288.
Intestinal putrefaction, 297, 298.
Intestine, large, absorption in, 302
    digestion in, 277, 298.
    extirpation of, 298.
    innervation of, 289, 290.
    movements of, 289.
  small, absorption in, 302 seq.
    digestion in, 294.
    extirpation of, 298.
    innervation of, 288.
    movements of, 286.
Iris, 527.
  innervation of, 528.
  movements of, induced from cortex, 658.
  protrusion of, in accommodation, 531, Fig. 226.
Iron, absorption of, 307.
  elimination of, 308.
  in chlorophyll, 24.
  in hæmoglobin, 152.
  in red blood corpuscles, 26.
Irritability, definition of, 50.
  of nerves, 410.
Island of Reil, 655, 662, Fig. 296; 668.
Isobutyl-amino-acetic acid, 70.
Isodynamic quantities of foodstuffs, 93.
Isolactose, 39.
Isolated conduction in nerves, 411.
Isomaltose, 246, 383.
Isometric contractions, 414.
Isotonic contractions, 415.
Isotonic solutions, 32.
Isthmus, rhombencephali, 600.

Jaw, lower movements of, in mastication, 278.
  in sucking, 279.
Jecorin, 79.
Jennings' theory of animal behavior, 55.

Keratin, 77.
  percentage composition of, 82.

Kidney extract, effect of injecting, intravenously, 368.
Kidneys, blood supply to, 385, Fig. 143.
  effect of removal of, 367, 390.
  internal secretion (?) of, 367.
  tubules of, 385, Fig. 144.
  vasomotor nerves of, 233, 235.
  volume of blood flow through, 240.
"Klopfversuch," 578.
Knee-jerk, 587.
Kymograph, 6, Fig. 1; 7.
  endless paper, 9, Fig. 6.
  long paper, 10.

Labor, 698.
Labor pains, 698, Fig. 302; 699, Fig. 303.
Laborers' rations, 141.
Labyrinth, membranous, extirpation of, in pigeon, 476, Figs. 187, 188, 189; see also *Semicircular canals, Cochlea, Otolith sacs.*
Lact-albumin, 701.
Lactase, 251.
Lactation period, 703.
Lact-globulin, 701.
Lactic acid, 155, 297, 373, 374, 376, 434, 447.
Lactose, 81.
Lagena, 473, 475.
Laked blood, 150.
Lampyris, 45.
Language faculties, 661.
  affected by lesions in cortex, 663, 664.
  how acquired, 661, 662.
  recovery of, after lesions in cortex, 665.
Lanolin, 80, 296.
Laryngeal muscles, 502.
Laryngeal nerves, inferior, motor for larynx, 324, 681.
  superior, 681.
    influence of, on respiratory movements, 330.
    motor for larynx, 324, 504.
Laryngoscope, 504.
Laryngoscopic picture, 504, Fig. 202; 505, Fig. 203.
Larynx, 502.
  control of, by cerebral cortex, 649, 650.
Latent period of contractions induced from cortex, 633, Fig. 283.
  of motor nerve endings, 418.
  of muscle, 415, 416, 424.
Lateral columns of the cord, 562, Fig. 254.
Lateral horn of the cord, 562, Fig. 254.
Lateral pressure, 202, 223; see also *Blood pressure.*
Laughing, 321.
Lecethin, chemical nature of, 78.
  elective solvent power of, 34.
  percentage composition of, 82.
Lecethin-albumins, 79.
Leech extract, 159, 351.
Leguminosæ, root tubercles of, 23, Fig. 18; 24.
Lemna triscula, 42, Fig. 25.
Leptoplana, 64, note.
Lesions of cerebellum, 608.
  of corona radiata, 647, 663.
  of frontal association center, 668.
  of midbrain, 613.
  of motor cortex, 645, 646, 660, 661.
  of posterior association center, 669.
  of sensory cortex, 650, 652, 653.
  of speech tract, 663, 664, 665.
  of spinal cord, 595.
  of temporal convolutions, 665.
  of 'tweenbrain, 617.
Leucin, 70, 72, 249, 255, 370, 374, 384.
Leucocytes, chemotaxis of, 54.
  formation of, 353.
  ingestion of foreign bodies by, 37, Fig. 22.
  movements of, described, 42, 43, Fig. 27.
  participation of, in absorption of proteid (?), 306.
  permeability of, to various solutions, 33.
  phagocytic function of, 37.
Leucomaines, 295.
Levator ani, 299.
Levatores costarum, 315.
Lever, recording, 6, Fig. 1; 7.
Levulose, behavior of, in diabetes, 363.
  properties of, 80.
  source of glycogen, 127.
Lieberkühn, glands of, 276, 277.
Liebig's classification of foodstuffs, 111.
Light, action of, on iris, 527, 528.
    on retina, 537.
  modifications of, 541.
  physical cause of, 536.
  physiological cause of, 453.
  production of, by living cells, 45.
  stimulation by means of, 56.
Light rays of solar spectrum, 536.
Light rays, relation of, to organ of vision, 541.
Lingual nerve as secretory nerve, 257.
  as vasomotor nerve, 234.
Lipolytic enzymes, 243.
  in pancreatic juice, 253.
  in stomach, 250.
Liquor follicularis, 695.
Listing's schematic eye, 511, 513, Fig. 210; 518.
Liver, blood supply to, 273, 274.
  exclusion of, from circulation, 227, 274, 371.
  extirpation of, in birds, 371.
  glycogen formation in, 375.
  regeneration of, 65.
  regulation of circulation by, 207, 227.
  secretion in, 272.
  sugar formation in, 375.
  urea formation in, 371.

Living substance, 15; see also *Protoplasm*.
  behavior of, in metabolism, 135, 137.
  constitution of, 20.
  form of, 15.
  impetus to formation of, 63, 64, note.
Load, effect of, on performance of muscle, 435, 446, 449.
Lobule, paracentral, 638, 639, Fig. 290; 652.
Localization, in retina, 518.
  in skin, 463.
  of temperature sense, 464.
  power of, affected by different conditions, 464.
Local sign, 463.
Locomotor movements, control of, by spinal cord, 586.
  in decapitated animals, 587.
Lophius piscatorius, 572.
Loudness of sound, 489.
Ludwig's air pump, 334, Fig. 130.
Lumbar nerves, innervation of urinary bladder by, 392, Fig. 145.
Lung catheter, 341, Fig. 133.
Lungs, see *Respiration* and *Respiratory movements*.
  circulation in, 227.
  elasticity of, 310.
  exchange of air in, 319.
  means of protection for, 323, 330.
  noxious air space in, 320.
  vasomotor nerves of, 233, 235.
  vital capacity of, 320.
Luteïn, 695.
Luteïn cells, 695.
Lymph, chemical properties of, 347.
  composition of, 348.
  definition of, 347.
  formation of, 349.
    filtration theory, 349, 350.
    secretion theory, 350.
  gases in, 348.
  medium for tissue cells, 30.
  movements of, 348.
  quantity of, formed in 24 hrs., 348.
Lymph glands, 352.
Lymph hearts of amphibia, 349.
Lymph vessels, contractions of, 349.
  valves of, 349.
Lymphocytes, 153.
Lymphogogic substances, 352.
Lymph-producing substances, 350, 351.
Lysin, 70, 72, 249.

Maculæ acusticæ, 475.
Magendie's doctrine, 565.
Magnesium, absorption and excretion of, 133.
  in bones, 26.
Magnesium salts, effect of, on ciliary movements, 25.
Magnesium salts, importance of, in plants, 24.
Malapterurus, 50.
Male sexual organs, 691.
Malic acid, 54.
Malleus of middle ear, 494, Fig. 196; 495.
  articulation of, with incus, 496, Fig. 198.
Malonic acid, 377.
Malpighian corpuscle, 386.
Malt sugar, 81; see also *Maltose*.
Maltase, 246, 251.
Maltose, 81.
  action of reversible enzyme on, 39.
Mammary glands, 703.
  fat in, 705.
  innervation of, 704.
  morphological changes in, 704.
Mannite, 80.
Mannose, 80.
Manometer, elastic, 9, Fig. 5.
  in determination of blood pressure, 202.
  mercury, 8, Fig. 3.
Marginal gyrus, 634.
Mariotte's experiment, 515, 516, Fig. 212.
Marrow, red, of bones, 150.
Marsh gas, 295.
Mastication, 278.
Maturity, period of, 706.
  sexual, 692, 696.
Maxwell's disks, 542.
Meals, 83.
Meat as article of food, 145; see also *Proteid*.
Mechanical stimulation, 56.
  of cortex, 633.
  of nerves, 418.
Medulla oblongata, or bulb, 600, 602.
  cardiac centers in, 195.
  functions controlled by, 604.
  importance of, 604.
  nuclei of cranial nerves in, 603, Fig. 269.
  respiratory center in, 325.
  transverse section of, 602, Fig. 268.
  various centers in, 602, 603, Fig. 269.
  vasomotor centers in, 238.
  vomiting center in, 286.
Meissner's plexus, 288, 687.
Membrane, animal, osmotic properties of, 32, 352.
  basilar, of organ of Corti, 499, 500, Fig. 199.
  of cells in general, 16.
  of plant cells, 21, Fig. 16.
  semipermeable, 31.
Memory, seat of, 671.
Memory pictures, 660, 663, 665, 669, 671.
Menstruation, cause of, 697.
  cosmic phenomena and, 62.
  description of, 696.
  physiological significance of, 697.
Mental work, influence of, on fatigue, 446, 676.
Mesencephalon, 600, 613.

Mesocarpus scalaris, 54, Fig. 31.
Mesoporphyrin, 152.
Mesoxalic acid, 377.
Metabolic products, 84.
  influence of, on organs, 356.
  removal of, by massage, 445.
Metabolism after extirpation of pancreas, 363.
    of thyroid, 360.
  after feeding thyroid extract, 361.
Metabolism, definition of, 83.
  effect of castration on, 357, 358.
  experiment in, example of, 91, 92.
  in different organs, 402.
  in fasting, 95.
  influence of age on, 119, 120.
    of food on, 98.
    of muscular work on, 110.
    of size of body on, 117.
    of temperature on, 114.
  intermediary, 373, 376, 377.
  in the young, 118, 119.
  methods of, 83 seq.
  of albumoses, 108.
  of alcohol, 110.
  of asparagin, 110.
  of carbohydrates, 105.
  of cellulose, 110.
  of fat, 104.
  of fatty acids, 109.
  of gelatin, 109.
  of gelatin-forming substances, 109.
  of peptones, 108.
  of proteid, 102.
  theories of, 134 seq.
Metacasein, 252.
Metallic taste, 484.
Metathalamus, 600.
Metencephalon, 600.
Methæmoglobin, 151.
Methyl-glyco-cyanamid, 382.
Methyl-indol-amino-acetic acid, 71.
Methyl mercaptan, 295.
Micturation, 390.
  center for, 393, 588.
Midbrain, 600, 613.
  importance of, in fishes, 619.
    in turtles, 621.
Middle ear, 494.
Milk, 700.
  coagulation of, 250.
  composition of, 701, 703.
  effect of, on properties of gastric juice, 265.
  secretion of, 703.
    influence of nerves on, 704.
    mechanism of, 704.
    quantity of, 705.
Milk sugar, 81; see also *Lactose*.
  origin of, 705.
Millon's reaction, 72.
Mind blindness, 669, 670.
Mind, mechanics of, 670, 673.
Mineral substances, see *Inorganic substances.*
  absorption of, 139, 307.
  in young animals and milk, 702.
  required by animals, 25, 26.
    by plants, 24.
Minimal air, 320.
Minimal requirements of food, 95.
  of proteid, 124.
Minimal stimulus, 51.
Mitral valve, 165.
Modalities of sensation, 453.
Moderate worker, nutritive requirements of, 142.
Molisch's reaction, 73.
Monamino acids, 70.
Monokow's bundle in the cord, 593, 596.
Monosaccharides, 80.
  percentage composition of, 82.
Moral significance of cerebral processes, 672.
Morphinism, 30.
Morphological changes during activity of gastric glands, 268.
  of hepato-pancreas of isopod, 244, Fig. 99.
  of intestinal glands, 277, Fig. 111.
  of mammary glands, 704.
  of nerve cells, 574.
  of pancreas, 272, Fig. 109.
  of retina, 537, 538, Fig. 232.
  of salivary glands, 260, Fig. 100; 261, Fig. 101.
Motility, forms of, 42.
Motor aphasia, 663.
Motor cortical areas, 633; see also *Cerebral localization.*
  action on, by other areas, 660, 661.
  connection of, with motor nerves, 594, Fig. 266; 647.
  development of, 648.
  extirpation of, in monkey, 644.
  finer movements dependent on, 644.
  in human brain, 645.
  psycho-physical significance of, 659.
  stimulation of, 601, 631, 632, 633.
    direct and crossed effects of, 640.
  suppression of, in dogs, 643.
    recovery of functions after, 646.
Motor nerves, 564.
Motor response in *Paramæcium*, 54, Fig. 32.
Motor sensations, 469.
  areas of, in cortex, 652.
  conducting tracts of, from cortex to cord, 647.
  in the cord, 596.
  physiological significance of, 472.
Motor sense, 462.
Motor spinal nerves, distribution of, 682, 685.
Motor zone of cortex, 634.

Mouth, digestion in, 290.
  sections of floor of, 281, Fig. 112.
Mouth cavity, closure of, in sucking, 279.
Movements, active, perception of, 471.
  associated, 473.
  coördination of, 473.
  passive, perception of, 469.
  voluntary, 449.
    how acquired, 450.
    regulation of, 472.
Movements of abdominal organs in respiration, 316, Fig. 125.
  of alimentary canal, 278.
  of diaphragm, 316, Fig. 125.
  of elementary organisms, 42.
  of eyes, 549; see *Eye movements.*
  of intestine, 286.
  of larynx, in deglutition, 281.
    in respiration, 312.
    in vocalization, 503.
  of œsophagus, 279.
  of ribs, 314.
  of stomach, 283.
  of vocal cords, in respiration, 312, 504, Fig. 202.
    in vocalization, 503, Figs. 200, 201; 505.
Muscle, cross-striated, functions of, 410.
    absolute power of, 438.
    action currents in, 48, 431.
    afferent nerves of, reflexes through, 470.
    blood supply to, 240, 449.
    central innervation of, 440.
    chemical changes in, due to activity, 434.
    chemistry of, 413.
    curves of, 7, 414, 415, 417; see also under *Curves.*
    degeneration of, 448.
    effect of veratrin on, 437, Fig. 175.
    elasticity of, 412, Fig. 150; 413, Fig. 152.
    electrical phenomena of, 47, 431.
    fatigue of, 441 seq.
    general properties of, 410.
    glycogen in, 81, 125, 374, 413.
    heat formation in, 402, 404, 439.
    latent period of, 415, Fig. 154; 416.
    mechanical work of, 435, Fig. 172.
    musical tone produced by contraction of, 434.
    permeability of, to solutions, 34.
    polar law of excitation of, 428.
    Pflüger's law of contraction of, 423.
    relation of, to other organs, 448.
    red and white, comparison of, 416.
    rigor of, 447.
    signs of activity in, 431.
    simple contraction of, 415; see also *Contraction.*
    stimulation of, 414.
    summation in, 415, 429.
Muscle, cross-striated, tetanus of, 429, Fig. 166; 430, Fig. 167; 433; see also *Tetanus.*
    tonus of, demonstration of, 581.
    variations in tension of, 414, Fig. 153.
    voluntary contractions of, 430.
    work done by single contraction of, 435.
    work done in tetanus of, 439.
  smooth, general physiology of, 447.
Muscles, see under individual names.
  skeletal, afferent nerves of, 470.
    motor nerves of, 682.
    tonus of affected by removal of semicircular canals, 477.
Muscular sense, 469; see also *Motor sensations.*
  cortical area of, 652.
Muscular work, CO_2 production in, 112.
  central nervous system and, 448.
  destruction of nonnitrogenous substances in, 112.
    of proteid in, 111.
  effect of, on circulation, 449.
    on digestion in stomach, 293.
    on formation of living substance, 63.
    on heart beat, 197.
    on respiration, 318.
  in tetanus, 439.
  maximum capacity for, in man, 447.
  metabolism in, 110.
  ratio of, to heat production in muscles, 440.
  regulation of, by muscles themselves, 437, 439.
Musical agraphia, 665.
Musical aphasia, 665.
Musical faculties, 665.
Musical tone, 489.
Mucin, 245.
  composition of, 82.
  in bile, 253.
  in saliva, 245.
Mucins, 74.
Mucoids, 74.
Mucous glands, 245.
  morphological changes in, 262, Fig. 102.
Myelencephalon, 600, 602.
Myelogenetic areas, of cerebrum, 666, Fig. 297; 667, Fig. 298.
Mylohyoid muscles, importance of, in deglutition, 280.
Myochrome, 414.
Myogen, 413.
Myogram, 8.
Myopia, 519, Fig. 215, 520.
Myosin, 413.
Myosinogen, 413.
Myristinic acid, 701.
Myxœdema, 358.
Myxœdematous woman, 359, Fig. 137.
Myxomycetes, 27.

N: C ratio in fæces, 90.
  in proteid, 92.
  in urine, 90.
Narcotics, physiological effect of, 65.
Nasal breathing compared with mouth breathing, 323.
Nasal cavity, closed in swallowing, 281.
  closed in vomiting, 286.
Native proteids, 73.
Nature, limits of knowledge of, 452.
Negative pressure in thorax, 310.
Negative variation, 433.
Nerve abducens, etc., see under individual names.
Nerve cells, central functions of, 566, 582.
  dependence of, on blood supply, 572.
  mode of reaction of, 570.
  morphological changes in, 574.
  nutritive functions of, 567.
  physiological stimuli of, 569.
  physiology of, 559 seq.
  regeneration and reproduction of, 574.
  rhythm of discharge of, 572.
Nerve centers, fatigue of, 676, 678.
  in spinal cord, 585; see also *Spinal cord.*
  in medulla oblongata, 603; Fig. 269; see also under individual names.
Nerve endings, of pain nerves, 467, 468.
  of pressure nerves, 461, 468.
  of temperature sense, 461, 468.
Nerve fibers, autochthonous, 575.
  autonomic, 686.
  degeneration in, 567.
  origin of, from nerve cells, 559.
  physiological differences between afferent and efferent, 565.
  pre-ganglionic and post-ganglionic, 686, 687.
  regeneration of, 564.
Nerve fibrils as conducting elements, 560, 585.
Nerve impulse, rate of transmission of, in motor nerves of lower animals, 417, Fig. 155.
    in motor nerves of man, 418.
    in spinal cord, 589.
Nerve processes, 559.
Nerves, accelerator, 191, 688.
  action currents in, 48, 431.
  afferent, 564, 565.
  alterations of excitability in, 425.
  anelectrotonus in, 425; Fig. 162.
  carbon dioxide formed in, 434.
  cardiac, 188 seq.
  catelectrotonus in, 424, Fig. 161.
  classification of, according to function, 564.
  depressor, of heart, 193, 681.
  efferent, 564, 565.
  electrical excitation of, 418.
    general law of, 420.
  electrolysis in, 434.
Nerves, fatigue of, 442, 443.
  general properties of, 410, 411.
  heat production in, 402.
  inhibitory, 188.
  intercostal, 324.
  isolated conduction in, 411.
  mechanical stimulation of, 418.
  motor, of bladder, 393.
    of stomach, 284, Fig. 114; see also *Stomach.*
    of throat, 282, Fig. 113.
  polar law of excitation of, 424.
  Pflüger's law of contraction of, 59, 423.
  promoting, 192.
  pulmonary, 681.
  rate of transmission in, 417, 418.
  signs of activity in, 431.
  special, physiology of, 680.
  specific response of, 411.
  spinal, 682.
  stimulation of, by induction currents, 426, Fig. 163.
    in arm of man, 427, Fig. 164.
  sympathetic, 685.
  trophic, 569.
  vasoconstrictor, 231, 582, 681, 685.
  vasodilator, 233, 234, 449, 681, 685.
Nervi erigentes, 393, 688, 693, 694, 700.
Nervous system, 31.
  central, 559.
  effect of different poisons on, 574.
  elemental structure of, summary, 561.
  influence of thyroid on, 360.
    of testes, 357.
  segmentation of, 575.
  sympathetic or autonomic, 686.
Network, intracellular, of nerve cells, 560, Fig. 252.
  pericellular, of Golgi, 561, Fig. 253.
Neuro-fibrils, 560, 585.
Neuron theory, 559.
Neurons, 559.
Neuropile, 560, 561.
Newborn, period of, 706.
  weight of, 706, 707.
Nicotin, use of, in tracing ganglionic connections, 582.
  in tracing vagus fibers, 190, 191.
Nitric-oxide hæmoglobin, 152.
Nitrogen, absorption of, by the blood, 335.
    by plants, 23, 24.
  channels of excretion of, 89, 90.
  determination of, in food and excreta, 83, 84.
  fixed by Bacteria, 24.
  in blood, 335.
  in digestive products of proteid, 295.
  in expired air, 89.
  in fæces, 90.
  in parotid gland, 259.
  in sweat, 89.

Nitrogen in urine, 89.
Nitrogen excretion, 89, 90.
  diurnal variations of, 102, Fig. 44.
  in starvation, 100, 101.
  proportional to N absorbed, 101.
Nitrogenous equilibrium, 91, 120, 121, 122.
  minimum proteid for, 103.
  on various quantities of proteid, 100.
Nitrogenous substances in the body, 68.
Nodal points of optical system, 511, Fig. 209.
  of schematic eye, 513, Fig. 210.
Nonnitrogenous foodstuffs, see *Carbohydrates* and *Fats*.
  destruction of, in muscular work, 112.
Nonnitrogenous substances in the body, 79.
Nonnucleated cells, 17.
Nubecula in urine, 380.
Nuclei of cranial nerves, 603, Fig. 269.
Nucleic acid, digestion of, 255.
  percentage composition of, 82.
Nuclein bases, 76; see also *Purin bases*.
Nucleins, 76, 351, 372.
  digestion of, 252, 255.
  percentage composition of, 82.
Nucleo-albumins, 75.
Nucleo-histon, percentage composition of, 82.
Nucleo-proteids, 77.
Nucleus, agency of, in activation of oxygen, 19, note.
  form and size of, 16.
  importance of, 17, 18.
  number in cells, 16.
  of cell, 16.
  of ovum, 695.
  reciprocal relations of, with protoplasm, 17.
  red, of tegmentum, 593.
Nucleus reticularis tegmenti, 603.
Nutrition, see *Food* and *Nutritive requirements*.
  definition of, 83, note, 137.
  of the brain, 676.
  of the heart, 180.
  of the young, 143.
  physiology of, 137.
Nutritive influence of cerebral cortex, 650.
  of nerve cells, 567, 568, 582, 584.
  of spinal ganglia, 584.
Nutritive requirements of adult males, 140.
  of persons of different ages, 144.

Occipital convolutions, 639, Fig. 289; 657.
Octave, 490.
Oculo-motor nerve, 680.
  accommodation and, 534.
  nuclei of, 535, Fig. 230; 615, Fig. 272; 616, Fig. 273.
  pupil and, 528.
Odors, classification of, 488.
  theories of transmission of, 486, 487.
Œsophageal fistula, 263.
Œsophagus, innervation of, 281.
  movements of, in swallowing, 280.
Ohm's law for analysis of sound, 493.
Oil and coagulation of blood, 159.
Old age, metabolism in, 120.
  period of, 706.
Oleic acid, 296.
Olein, 79, 701.
Olfactometer, 487, Fig. 192.
Olfactory areas in the cortex, 653.
Olfactory cells, 487.
Olfactory epithelium, 486.
Olfactory lobe, 600, 619.
Olfactory nerves, action of, on respiration, 330.
  specific, of smell, 488.
Opalina ranarum, 61, Fig. 35.
Opening contraction, 420, 423.
Opening period of parturition, 698.
Operative interference, 5.
Optic cortex, activity of, 660.
  connections of, 660, 662, Fig. 296; 663.
  efferent fibers from, 657.
Optic lobes, Figs. 274, 275, 276, 277, 278.
  equivalent to corpora quadrigemina, 613; *which also see*.
Optic nerve, 330; 535, Fig. 230: 656, Fig. 295; 657, 680.
  efferent fibers in, 515, Fig. 211.
  reflex effect of, on respiration, 330.
Optic thalamus, 600.
  effect of lesions in, 617.
  substitution of functions in, 617.
Optic tracts, schematic representation of, 535. Fig. 230; 656, Fig. 295.
Optical axis, 513, Fig. 210; 525.
Optical constants of the eye, 508.
Optical defects of the eye, 520.
Optical system, nodal points of, defined, 511, Fig. 209.
  of the eye, 509, 510.
Optical zone of the cornea, 522.
Optogram, 537.
Organ of Corti, 499, 500, Fig. 199.
Organ system, definition of, 30.
Organic foodstuffs, 83.
Organic sensations, 469.
Organs, coöperation of, 30.
  influence of, on one another, 1, 355.
  surviving, 6.
Orientation, importance of otolith sacs for, 473, 481.
Oscillaria, 29.
Osmosis, 31.
Osmotic phenomena, significance of, for absorption, 35, 301, 353.
    for different organs and tissues, 34, 355.
    for elementary organisms, 33, 34.
    for excretion, 41.
    for lymph formation, 349.

Osmotic phenomena, significance of, for production of urine, 387.
Osmotic pressure, definition of, 31.
Osmotic tension in animal cells, 35.
  in plant cells, 33.
Osseïn, 78.
Ossicles of middle ear, 495.
Otolith, 481.
Otolith sacs, functions of, 481.
Ovaries, 695.
  internal secretion of, 358.
Overtones, definition of, 491, 492, Fig. 194.
  in human voice, 505.
Oviduct, 695.
Ovovitellin, 79.
Ovulation, 696.
Oxalic acid, 41, 376, 377, 383.
Oxidation, 27; see also *Combustion*.
Oxidative processes in cells, 39.
Oxyacids, aromatic, 378.
Oxybenzuric acid, 378.
Oxybutyric acid, 376, 384.
Oxyethyl-trimethyl-ammonium hydroxide, 78.
Oxygen, absence of, effect on eggs of, 26.
    behavior of frogs in, 27.
    suitability of, for certain Bacteria, 28.
  absorption of, by blood, 336, 337, Fig. 131.
    total in man, 346.
  activation of, 19, note.
  amount of, absorbed under different circumstances, 346.
    consumed by elementary organisms, 27.
  coefficient of absorption of, 336.
  combination of, in blood, 336.
  determination of, in blood, 334, Fig. 130; 335.
    in metabolism experiments, 86, 88.
  distribution of, in blood, 340.
  importance of, for development, 26, 27.
  increased consumption of, in fatigue, 446.
  partial pressure of, in alveolar air, 336.
  percentage of, in arterial and venous blood, 339.
    in expired air, 343.
    in inspired air, 342.
  stored in loose compounds, 27.
  tension of, in blood, 341.
    in lymph, 348.
Oxyhæmoglobin, 150, 151.
  absorption spectrum of, 151, Fig. 47.
Oxymonamino acids, 70.
Oxyphenyl-amino-propionic acid, 71.
Oxyproteïc acid, 373, 382.
Oxypyrimidin, 76.
Oxypyrrolidin-carboxylic acid, 72.

Pain, 465.
  after hemilesion of the cord, 597.
  area for, in cortex, 652.
Pain, end organs of, 468.
  nerves, (?) 467.
  physiological cause of, 466.
  tract for, in the cord, 597.
Pain points in the skin, 467.
Pains, labor, 698, Fig. 302.
Palæmonetes, 60, Fig. 34.
Pallium of the brain, 600.
Palmitic acid, 79.
Palmitin, 79, 701.
Pancreatic diabetes, 127, 128, 362, 375.
Pancreatic fistula, 243, 251.
Pancreatic juice, 251.
  action of, on carbohydrates, 251, 297.
    on fats, 253, 295.
    on proteids, 252, 294.
  enzymes in, 251, 271, Fig. 108.
  influence of bile on, 251, 294.
    of food on, 270, Fig. 107; 271, Fig. 108.
  properties of, 251.
  secretion of, 269.
    daily course of, 270, Figs. 106, 107.
    nervous control of, 269.
Pancreas, effects of extirpation of, 127, 362, 375.
  internal secretion of, 362.
  morphological changes in, 272, Fig. 109.
  specific excitants of, 270, 271.
Papillary muscles, action of, 166.
Paracasein, 250.
Paracentral lobule, 638, 639, Fig. 290; 652.
Paracresol, 379.
Paracresol-sulphuric acid, 379.
Paralactic acid, 155.
Paralysis, definition of, 50, 65.
  following partial destruction of the cord, 596.
  following removal of motor cortex, 644.
Paramæcium, chemotaxis of, 55.
  directive influences on, 55, 59, note.
  electrical stimulation of, 59.
  geotaxis of, 56.
  motor response of, 55, Fig. 32.
  starvation of, 28.
  thermotaxis of, 59.
  thigmotaxis of, 56.
Paramyosinogen, 413.
Paranuclein, 75.
Para-phenyl-amino-propionic acid, 71.
Parenchyma cells of root cortex, 21, Fig. 16.
Parietal cells, 267.
  secretion capillaries of, 267, Fig. 105.
Parietal convolutions, see *Central convolutions*.
Parietal lobes, 624, Fig. 280; 645.
Parotid glands, innervation of, 257, 258.
  morphological changes in, 260, Fig. 100; 261, Fig. 101.
Paroxy-benzuric acid, 378.
Paroxy-phenyl-acetic acid, 378.
Paroxy-phenyl-propionic acid, 378.
Pars mamillaris hypothalami, 600.

Pars optica hypothalami, 600.
Partial pressure of gases, 334.
Parturition, 691, 697.
Passive movements, perception of, 469.
Pathogenic bacteria, ingestion of, by leucocytes, 37.
Pathology, relation of, to physiology, 4.
Pectorales as muscles of respiration, 316.
Peduncles of the cerebellum, 593, 612.
Pelomyxa, 57.
Pendulum hydrometric, 210.
Pendulum movements of the intestine, 287.
Penis, 692, 693.
Penta-methyl-endiamin, 249.
Pentoses, 81.
Pepsin, formation of, 267.
  properties of, 248.
Pepsin-hydrochloric acid, action of, 291.
Pepsinogen, 248.
Peptoids, 249.
Peptones, 75, 249, 255, 351.
  food value of, 108.
  intestinal juice and, 255.
Peptozymes, 250.
Pericardium, rôle of, in action of heart, 177.
Perilymph, 495.
Period of ejection of the heart, 171.
  of relaxation of muscular contraction, 416.
  of rising tension of the heart, 171.
  of shortening of muscular contraction, 416.
  refractory, of heart, 183.
    of nerves, 429.
    of nerve cells, 572.
Peripheral ganglia, 583, 584, Figs. 258, 259.
Periphery of retina, adaptation of, to light and dark, 540.
  color vision with, 546.
  vision with, 514.
Periplaneta, 56.
Peristalsis, 288.
Permeability of blood corpuscles, 33, 34.
  of cross-striated muscles, 34.
  of living and dead membranes, 34.
Perspiration, see *Sweat*.
  insensible, 394, 397.
Pflüger's law, 423.
Phagocytosis, 37, 54.
Pharynx, action of, in swallowing, 280.
Phenol, 295, 378, 379.
Phenolphthalein, 147, 379.
Phenol-sulphuric acid, 379.
Phenyl-acetic acid, 378.
Phenylalanin, 71, 72, 249.
Phenyl-propionic acid, 378.
Phlebin, 150.
Phloridzin, 127, 374, note, 375.
Pholas, 45.
Phospho-carnic acid, 413.
Phosphorescence, 45.
Phosphorus, absorption of, 132.
  excretion of, 132.
  in iodothyrin, 362.
  in proteids, 75, 76, 82.
Phosphorus poisoning, 129.
Photography, registration by, 13.
Phototaxis, 57.
Phrenic nerve, 324, 331.
Phrenology, 630.
Phylloporphyrin, 152.
Physical methods of investigation, 4.
Physiological salt solution, 53.
Physiology, general and special, 15.
  province of, 2.
Pigment granules, 22.
Pigments in the bile, 253.
  in the blood, 150.
  in the eye, 527, 537.
  in muscle, 414.
  in urine, 383.
Pilocarpine and formation of urine, 389.
Pilomotor fibers, 687, 688.
  connection of, with ganglion cells, 582.
Pineal body, 600, 613.
Pitch of sound, 489.
  of human voice, how caused, 505.
Pituitary body, internal secretion of, 367.
Placenta, 698.
Plasma, chemical constitution of, 154.
Plasmolysis, 33.
Plastic foodstuffs, 111.
Platelets of the blood, 153.
Plethysmograph, 211, Fig. 83.
Plethysmographic curve, 212, Fig. 84.
  in sleep, 677, Fig. 299.
Plexus, cardiac, 191, Fig. 67.
  hypogastric, 392, Fig. 145; 393, 694.
  myentericus, 288.
  of Auerbach, 284, Fig. 114; 288, 687.
  of Meissner, 288, 687.
  vesical, 392, Fig. 145.
Pneumographic curve, 313, Fig. 121.
Poikilothermous animals, 46, 442.
Poisons, physiological significance of certain, 574.
Poisonous constituents in expired air, 344.
Poisseuille's formula, 222.
Polar law of excitation, 424.
"Polar failure" of excitation, 428.
Polarizing current, 425, 434.
Polysaccharides, chemical constitution of, 82.
  properties of, 81.
Polystomella, 17, Fig. 14.
Pons, 600, 612.
Portal circulation, 137, 162.
Portal vein, 162; see also *Eck fistula*.
Position of the body, influence of, on flow of blood, 226, Figs. 93, 94; 227.
  perception of, 469, 481.

Posterior columns of the cord, 562, Fig. 254.
Posterior horn of the cord, 563.
Posterior roots of the spinal nerves, 563, 564, 566.
Postganglionic fibers, 687, 688, 689.
Potassium salts, effect of, on heart, 25.
    on smooth muscle, 25.
  importance of, in plants, 24.
  toxicity of urine due to, 381.
Potential, electrical differences of, 47, 418.
Potential energy of foodstuffs, 92; see also *Energy*.
Precipitins in the blood, 156.
Preganglionic fibers, 686, 689.
Pregnancy, 697.
Presbyopia, 530.
Pressure, abdominal, 299, 699.
  in the mouth cavity, 279, 280.
  in the respiratory passages, 321.
  intracardial, 169, Fig. 56; 170, Fig. 57; 171, Fig. 58; 173, Fig. 60.
  intracranial, 678.
  intrathoracic, 228, 310.
  intrauterine, 698, Fig. 302; 699, Fig. 303.
  of the blood, see *Blood pressure*.
  osmotic, 31; see also *Osmotic phenomena*.
Pressure points or spots in the skin, 459, Fig. 182; 462.
Pressure sensations, 458, 461.
  application of Weber's law to, 456.
  local sign of, 463.
Pressure sense, 461.
  area for, in cortex, 652.
  end organs of, 468.
  nerves of, 461.
  tract for, in the cord, 597.
Primary follicle, 695.
Primordial myelogenetic regions of the cortex, 667.
Primordial ova, 695.
Primordial sheath, 33.
Products of metabolism, see *Decomposition products*.
Projection of sensations in general to the external world, 454.
  of visual sensations to the external world, 552.
Projection fibers of the brain, 667.
Promoting nerves of the heart, 192.
Prosencephalon, 600.
Prostate, 691.
Prosthetic group in compound proteids, 75.
Protagon, 79.
Protamins, 70, 77.
Protection, against loss of heat, 404.
  insured by blood, 157.
  means of, for lungs, 323, 324.
Proteid, absorption of, 305.
  amount of, in daily ration, 142.
Proteid, chemistry of, see *Proteids*.
  circulating, 134.
  decomposition of, in body, 369.
  determination of, in food, 83, 84.
  importance of, in metabolism, 98.
  in urine, 384.
  metabolism of, 99.
    in fasting, 97.
    in muscular activity, 112.
    influence of body mass on, 117.
    influence of, on total metabolism, 102.
    proportional to proteid ingested, 99.
    with carbohydrates, 105.
    with fats, 104.
  physiological heat value of, 93.
  putrefaction of, in intestine, 378.
  relation of, to living substance, 20.
  requirements, different views on, 142.
  retention, 120.
    in growing body, 123.
  source of fat in the body, 129, 130.
  source of glycogen, 127.
  synthesis of, in animals, 25.
    in plants, 23.
  tissue, 134.
  utilization of, 138.
Proteids, action of digestive fluids on, 248, 252, 255.
  as constituents of dead protoplasm, 20.
  atomic groups in, 70.
  carbohydrate groups in, 71.
  chemical constitution of, 69, 70, 82.
  color reactions for, 72.
  compound, 75.
  conjugated, 75.
  crystallized, 68, 69, Fig. 38.
  formation of, in plants, 23.
  modified, 68.
  native, 69.
  of blood, 154.
  of milk, 701, 703.
  origin of, 23.
  percentage composition of, 82.
  physiology of, see under *Proteid*.
  phosphorus-containing, 75, 76.
  precipitants of, 69.
  properties of, 68.
  salted out, 69.
  simple, 75.
  solubility of, 68, 69.
Proteolytic enzyme, 243.
  in intestine, 255.
  in pancreas, 252.
  in stomach, 248.
Proteoses, 250.
Protoalbumose, food value of, 108.
Protoplasm, appearance of, 20.
  chemical constitution of, 20.
  chemical nature of, 68.

Protoplasm, chemical and physical properties of, 19.
  decomposition products of, 68, 70, 249.
  differentiations of, 16.
  formation of, in animals, 25.
    in plants, 23.
  inclosures in, 21, 22.
  morphology of, 20.
  motility of, 42.
  osmotic properties of, 31 seq.
  power of, to store oxygen, 27.
  relation of, to nucleus, 17.
  state of aggregation of, 19.
Protoplasmic processes, 42.
  of nerve cells, 559.
Pseudoglobulin, 154.
Pseudohæmoglobin, 152.
Pseudonuclein, 75.
Pseudopodia, 36, 42.
  of *Amœba*, 35, Fig. 20; 36, Fig. 21; 42, 43.
  of Gromia oviformis, 35, Fig. 19.
  of Polystomella venusta, 17, Fig. 14.
  of Thalassicola nucleota, 18, Fig. 15.
Psychical activities, organs of, 666.
  substratum of, 629.
Psychical disturbances after extirpation of thyroid, 361.
Psychical influence over reflexes, 577, 579.
Psychology of Gall, 629, 630.
Psycho-physical events, time required by, 673.
Psycho-physical functions of the cerebrum, 658.
Pterygoid muscles in mastication, 278.
Ptyalin, 245, 246.
Puberty, in the male, 692.
  in the female, 697.
  influence of, on growth, 708, 709, 710
Pulmonary arteries, 161.
  pressure in, 228.
Pulmonary circulation, 227 seq.
Pulse, arterial, 212.
  venous, 234.
Pulse curve, 12, Fig. 11; 216, Fig. 88.
Pulse rate, see *Heart beat.*
  as affected by food, etc., 197.
  at different ages, 197, Fig. 71.
Pulse volume, 204.
  dependence of, on flow from great veins, 184.
Pupil, constriction of, 528.
    by cortical stimulation, 658.
    center for, 529.
  dilatation of, 528.
    by cortical stimulation, 658.
    center for, 529.
Purin bases, 76, 255, 372, 382.
Purkinje's figure, 516.
Putrefaction in the intestine, 297, 298, 378.
Putrefactive products, 295, 378.
Putrescin, 249.
Pyloric fistula, 267.
Pyloric glands, 266.
Pylorus, innervation of, 284, Fig. 114.
  movements of, 283.
Pyramidal cells of the cortex, 634, Fig. 284.
Pyramidal tracts in the cord, 593, 595, 596, 647, 648.
Pyrimidin, 76.
Pyrrolidin-nucleus, 71.
Pyrrolidin-carboxylic acid, 71, 72, 249.

Qualitative relations between stimulus and sensation, 451.
Quantitative relations between stimulus and sensation, 455.
Quotient, respiratory, 105, 343.

Radiation of heat, 403.
Radium, 58.
Rami communicantes, 687, 689
Ration, Voit's, 142.
Ration for woman, 143.
Reaction time, 673.
  as effected by fatigue, etc., 674.
  discrimination, 676.
  muscular, 675.
  simple, 673.
  to different sensory stimuli, 674.
Receptaculum chyli, 349.
Recovery after fatigue, 66.
  of muscle, 445, 446.
  of nerve, 443.
  of visual organ, 539.
Recovery of muscular functions after destruction of cortex, 646.
Rectum, innervation of, 289.
  reflex induced from, 299.
Recurrent fibers, 584.
Recurrent sensibility, 566.
Red blindness, 546.
Red blood corpuscles, see under *Blood.*
Red-green blindness, 547.
Reduced eye, 512.
Reducing substance in urine, 383.
Referred pains, 689.
Reflection of pulse waves, 214, 218.
Reflex, causing ejaculation, 693.
  contractions, 571, Fig. 256.
  definition of, 411, 570.
  fall of blood pressure, 237, Fig. 98.
  origin of tonus, 581.
  processes, 575.
  responses to different stimuli, 580.
  rise of blood pressure, 236, Fig. 97.
  stimulation of nerve cells, 570, 571.
  touch, 660.
Reflexes, axon, 584, Fig. 258.
  augmentation of, 579.
  facilitation of, 579.

Reflexes, flexor and extensor, 587.
  from heart, 194.
  general features of, 576.
  inhibition of, 577.
  locomotor, 617.
  purposive, 577, 586.
  psychical influence over, 577.
  reënforcement of, 579.
  regulative, 576.
  respiratory, 327.
  segmental, 576.
  suppression of, 578, 579.
  tendon, 587.
  through sympathetic ganglia, 583.
  to different stimuli, 580.
  to heart, 193.
  to pancreas, 270.
  to salivary glands, 260.
  to stomach, 263.
  vasomotor, 235.
Refraction, angle of, 509.
  in eye, 510.
  of light, 508.
  static, in eye, 519.
Refractory period of heart, 183.
  of nerve cells, 572.
  of nerves, 429.
  of skeletal muscle, 429.
Regeneration, 64.
  determining factor in, 64, note.
  in sympathetic system, 689.
  of kidney tissue, 65.
  of liver tissue, 65.
  of nerve tissue, 574.
Registers of voice, 504.
Registration, see *Graphic method*.
  by air-transmission, 11.
  by photography, 13.
Regulation of blood pressure, 194, 219.
  of heart activity, 186, 194.
  of respiration by vagi, 327.
  of temperature in body, 406.
Regurgitation of blood, 166, 167.
Rennin, 250.
Reproduction, physiology of, 691.
  post-embryonic, of nerve cells, 574.
Reserve air, 320.
Residual air, 320.
Resistance in arteries, 205.
  to conduction in nerves, 411, 425, 426.
  to electric current, 418, Fig. 156.
  to fatigue of nerves, 442.
Resonance, 492.
Resonance theory of hearing musical sounds, 498.
Resonance tone of external auditory meatus, 494.
  objections to, 501.
Resonator of Helmholtz, 493, Fig. 195.
Resonators of cochlea, 498.
Respiration, action of various efferent nerves on, 330.
  artificial, 5, 231, 325.
  effect of suction in thorax on work of, 312.
  exchange of air in lungs in, 319.
  heat loss and, 403.
  influence of higher brain centers on, 329.
  innervation of, 323.
  movements of, 310.
  muscular work and, 318.
  periodic variations in, 333.
  regulation of, by vagi, 327.
  residual air, reserve air, etc., of, 320.
  types of, 318, Fig. 126; 333.
Respiration apparatus, of Atwater and Benedict, 86.
  of Pettenkoffer, 86.
  of Pettenkoffer and Voit, 87, Fig. 41; 88.
  of Sondén and Tigerstedt, 88, Fig. 42; 89.
Respiration calorimeter, 86, Fig. 40.
Respiratory center, 325.
  normal stimulation of, 331.
  resistance of, to asphyxiation, 573, Fig. 257.
Respiratory centers, spinal, 325, 326.
Respiratory curve of rabbit, 314, Fig. 123; 328, Fig. 129.
Respiratory exchange of gases, 340.
  amount of, 345.
Respiratory foods, 111.
Respiratory movements, 310.
  concomitant, 321.
  effect of, on blood pressure, 227.
    on heart, 176.
  force of, 322.
  innervation of, 323.
  number of, 318, 319, Fig. 127.
    registration of, 312.
  special forms of, 321.
Respiratory nerves, 324.
Respiratory passages, 310, 323.
  ciliated epithelium in, 323.
  pressure variations in, 321.
Respiratory products, 89, 342.
Respiratory quotient, 105, 343.
  use of, in metabolism experiments, 105.
  values of, under different circumstances, 343.
Respiratory reflexes, 327.
Respiratory sounds, 322.
Respiratory system, 31.
Respiratory variations of blood pressure, 229, Fig. 95; 230, Fig. 96.
Restitution after lesions of cortex, 646.
Retention of proteid, 120.
  in growing body, 123.
Reticulin, 78.
  percentage composition of, 82.
Reticulum of the neuropile, 560, 561, 585.

Retina, action current in, 537.
  adaptation of, 540.
  centrifugal fibers to, 515, Fig. 211.
  excitation of, 536 seq.
  fatigue and recovery of, 539.
  histological structure of, 515, Fig. 211.
  images upon, 513.
  light-perceiving layer of, 514.
  morphological changes produced in, by light, 537, 538, Fig. 232.
  relation of properties of light to different constituents of, 541.
Retinæ, correspondence of, 555.
  projection of, on cortex, 655.
  rivalry of, 555, Fig. 247; 556.
Retinal images, 511, 513.
  relation of, to tactile impressions, 556.
  size of, 554.
Retinal pigment, 541.
Retinal vessels, shadows of, 516.
Rheocord, 418, Fig. 156.
Rheotactic influence on spermatozoa, 697.
Rheotaxis, 56.
Rheotome experiment, 431, Fig. 168.
Rheotome of Bernstein, 432, Fig. 169.
Rheotropism, 64.
Rhinencephalon, 600.
Rhizopoda, 37.
Rhombencephalon, 600.
Rhythmical contractions of cross-striated muscle, 53.
Rhythmical segmentation, 287, 288, Fig. 116.
Rib-lifting muscles, 315.
Ribs, movements of, 314.
Rigor mortis, 447.
Ringer's solution, 25 note; 182.
Rise of temperature, effect of, on lower organisms, 29.
  in human body, 401.
Ritter's tetanus, 421.
Rivalry of retinæ, 555, Fig. 247; 556.
Rods and cones, 515, Fig. 211.
  functions of, 541.
Röntgen rays, 58.
Root tubercles, 23, Fig. 18; 24.
Rotation, an effect of removing cerebellum, 608.
  in protoplasm, 42.
Rotation axes of eye, 549, 550, Fig. 240.
Rotation center of the eye, 549.
Round window, 497.
Rubro-spinal tract in the cord, 593, 595.

Saccharinic acid, 374.
Saccharose, 81.
Sacculus of internal ear, 473.
Sacral nerves, 392, Fig. 145; 393.
Salicylic acid, 378.
Salicyluric acid, 378.
Saliva, 245, 246.
Salivary glands, 257.
  electrical phenomena of, 48, 257.
  morphological changes in, 261.
  nerves of, 257, 258.
    centers for, 261.
  specific excitants of, 260.
Salt, common, physiological importance, 25.
  physiological solution of, 53.
Salt hunger, 131.
Salt plasma, 157.
Salt taste, 484.
Salting out, 69.
Salts, required by animals, 25, 26; see also *Inorganic substances* and *Constituents, inorganic*.
  by heart, 25, 182.
  by plants, 24.
Sap of plant cells, 21, Fig. 16; 33.
Saponification equivalent of fats, 79.
Sarcolactic acid, 376.
Sarcolemma, 16.
Saturation of color, 541.
Scaleni muscles, 315.
Scheiner's experiment, 553, Fig. 243.
Schematic eye, 511, 513, Fig. 210.
Schwann's experiment, 439.
Scyllium canicula, brain of, 619, Fig. 275.
Season, influence of, on growth, 710.
Sebaceous glands, 394.
Sebum, 394.
Secondary contractions, 433.
Secondary sexual characters, 357.
Secondary tetanus, 433.
Secretin, 271.
Secretion, as a process, definition of, 41.
  conditions for, in stomach, 265.
  filtration theory of, 259.
  in intestinal glands, 276.
  in pancreas, 269.
  in salivary glands, 257.
  in sebaceous glands, 394.
  internal, 356; see also *Internal secretion*.
  of bile, 272.
  of digestive fluids, 256.
  of sweat, 396.
  paralytic, 259.
  psychical, 263.
Secretion as a product, see under individual names.
Secretion capillaries, 267, Fig. 105.
Secretion droplets, 244, Fig. 99.
Secretion vacuoles, 261, Fig. 101.
Secretory nerves, 564, 681; see also under different glands.
Segmental reflexes, 576.
Segmentation of central nervous system, 575.
Selachians, extirpation of cerebrum in, 619.

Self-consciousness, origin of, 672.
Self-digestion of the stomach, 269.
Self-regulation of respiratory movements, 328.
Semicircular canals, 473.
  artificial stimulation of, 479.
  experimental suppression of, 476, Figs. 187, 188; 477, Fig. 189.
Semilunar valves, 167.
  closure of, 171.
  muscular supports of, 167.
  opening of, 171.
Seminal fluid, 692, 693, 694.
Seminal vesicles, 692.
Semipermeable membrane, 33.
Semipermeable walls, 31.
Senescence, 66.
Sensations, auditory, 489.
  correspondence of, to reality, 452.
  definition of, 451.
  degrees of distinction of, 453.
  gustatory, 483.
  modalities of, 453.
  motor, 469.
    physiological significance of, 472.
  of color, 541.
  of pain, 458, 465.
  of position, 472, 473.
  of pressure and touch, 458, 461.
  of resistance, 461, 471.
  of temperature, 458.
  of weight, 456, 471.
  olfactory, 486.
  organic, 454, 469.
  place of origin of, 454, 659.
  qualitative relations of, to stimuli, 451.
  quantitative relations of, to stimuli, 455.
  specific, doctrine of, 455.
  tactile, 461, 466, 652.
  theoretical explanation of, 453.
  threshold stimuli of, 455.
  tickling, 462.
  transcendental, in essence, 455.
  visual, 536.
  Weber's law concerning, 456.
Sense of cold, 459.
  of force, 460.
  of hearing, 498.
  of heat, 459.
  of motion, 452.
  of pain, 465.
  of position, 469.
  of pressure, 461.
  of sight, 508.
  of smell, 54, 486.
  of taste, 483.
Senses, classification of, 451, 452; see also *Sensations*.
Sensory aphasia, 664.
Sensory areas of cortex, 650.
Sensory areas of cortex, connected together, 659.
  general sensation and touch in, 654, Figs. 293 and 294.
  hearing in, 654, Fig. 293.
  psycho-physical significance of, 659.
  recapitulation concerning, 658.
  taste and smell in, 653, 654, Fig. 294.
  vision in, 654, Fig. 293.
Sensory impressions, conduction of, in cord, 597.
Sensory spinal nerves, 682.
  distribution of, 683, Fig. 300.
Serin, 70, 72.
Serous cavities, absorption from, 353.
Serrati muscles, 316.
Serum, 154.
  agglutinating action of, 156, 157.
  bacteriocidal action of, 155, 156.
  CO_2 in, 340.
  cytolytic action of, 156.
  mineral substances in, 154.
  organic substances in, 154, 155.
  oxygen in, 340.
Serum albumin, 154.
Serum globulin, 154.
Sex, influence of, on heart beat, 197.
    on metabolism, 144.
Sexual glands, accessory, 691, 692.
Sexual maturity, in man, 692.
  in woman, 696.
Sexual organs, female, 695.
  male, 691.
Shock, effect of, in experiments on respiration 326.
    in lesions of motor areas, 646.
Shrimp, galvanotaxis of, 60, Fig. 34.
Sighing, 321.
Sight, sense of, 451; 508; see also *Vision* and *Eye*.
  cortical area for, 655.
  reaction time to, 674.
Sigmoid flexure of colon, 299.
Sigmoid gyrus, 266, 632, Fig. 282.
Signal, electric, 10, Fig. 7.
Simultaneous contrast, 547.
Sinuses of Valsalva, 167.
Siren, Seebeck's, 490, Fig. 193.
Size, judgment of, by vision, 554, Figs. 244, 245, 246.
Skatol, 295, 378, 379.
Skatoxyl, 379.
Skatoxyl-sulphuric acid, 379.
Skeletal muscles, see *Muscles*.
Skin, electrical phenomena of, 48.
  excretory functions of, 394.
  glands, stimulation of, by alkalies, 59.
  heat loss by, 395, 403.
  insensible perspiration of, 397.

Skin, sensory functions of, 458.
  temperature of, 399.
Sleep, 676.
  curve of depth of, 677, Fig. 299.
  effect of loss of, on fatigue, 445.
  Howell's theory of, 677.
  metabolism in, 676.
Small intestine, see *Intestine, small.*
Smell, see *Olfactory sensations, Odors,* etc.
  as a chemical sense, 54.
  cortical area for, 653, 654, Fig. 294.
  definition of, 451, 483.
  quantitative capacity of, 488.
Sneezing, 321.
Soaps as fat producers, 130.
Soaps in intestine, 295.
  injected into blood, 305.
Sobbing, 321.
Sodium chloride, excretion of, in starvation, 131.
  importance of, for heart, 25, 182.
  osmotic pressure of, 32.
Sodium glycocholate, 254.
Sodium taurocholate, 254, 351.
Solar spectrum, see *Spectrum.*
Sorbite, 80.
Sound, cardiographic, 168, Fig. 55.
  qualities of, 489, 491; see also under *Ear.*
  transmission of, in ear, 493.
Sounds, respiratory, 322.
Sounds in swallowing, 282.
Sounds of heart, 167, 168.
Special nerves, physiology of, 680.
Specific action of enzymes, 38, 39.
Specific affinities in absorption, 35.
Specific dynamic action of foodstuffs, 107.
Specific excitants of digestive glands, 264, 271, 275.
Specific gravity, changes of, in elementary organisms, 45.
  of blood, 147.
  of sweat, 395.
  of urine, 380.
Specific response, law of, in nerves, 411.
Specific stimuli for end organs, 580.
Spectrum, visible rays of, 536.
Speech, center of, 631.
  elements of, 506.
  powers of, 661, 662.
  tract in cortex, 662, Fig. 296.
Spermatozoa, 691, 692.
  chemotactic influence on, 54, 697.
  thigmotactic influence on, 56, 697.
Spermatozoids of fern, chemotaxis, 54.
Spherical aberration, 523, Fig. 218; 522.
Sphincter ani, 299.
  innervation of, 299.
  tonus of, 583, 588.
Sphincter of urinary bladder, 391.
  innervation of, 393.
Sphincter pupillæ, innervation of, 528.
Sphygmogram, see *Pulse curve.*
Sphygmograph, 215, Fig. 87.
  spring of, 214, Fig. 86.
Sphygmomanometer, 202, 203, Fig. 76.
Spinal accessory nerve, 681.
Spinal cord, centers in, 585.
  columns of, 562, Fig. 254; 589, Fig. 261; 591, Fig. 264; 592, Fig. 265; 593.
  conducting pathways in, 588.
    afferent, 592, Fig. 265; 593, 595, 596.
    efferent, 593, 594, Fig. 266; 595.
    motor, 594, Fig. 266.
    sensory, 592, Fig. 265.
  control of skeletal muscles by, 586.
  electrical stimulation of, 588, 590, Fig. 263.
  extirpation of, 581, 582, 587.
  hemisection of, 595, 596, 640.
  influence of, on vegetative organs, 587.
  rate of propagation in, 589.
  section of, 588, 595, 597.
  structure of, 562, Fig. 254; 563, Fig. 255.
Spinal ganglia, 563, Fig. 255.
  chief purpose of, 584.
  delay of impulse in, 585.
Spinal nerves, 682.
Spinal nerve roots, 562, 564.
  efferent fibers in posterior, 566.
  various functions of, 565.
Spirogyra, 18.
Spirometer, 320, Fig. 128.
Splanchnic nerve, 688; see also *Sympathetic nerves.*
  as secretory nerve of pancreas, 269.
  as vasomotor nerve, 233, 235.
  connection of, with ganglion cells, 582.
  intestinal movements and, 288.
  movements of stomach and, 284.
  respiration and 331.
Spleen, function of, 368.
  trypsin and, 252.
Spongioplasm, 19.
Spontaneous generation, 16.
Squalius cephalus, brain of, 618, Fig. 274.
Squint, 555.
Stapedius muscle, 494, Fig. 196; 497.
Stapes, 494, Fig. 196; 496.
Staphylococcus pyogenes albus, 54.
Starch, see *Carbohydrates.*
  absorbed, 139.
  action of saliva on, 246.
  digestion of, in intestine, 251, 297.
    in mouth, 291.
    in stomach, 291.
  formation of, 23.
  kinds of, 81.
Starch cellulose, 81.

Starch granules in food, 242.
Starch granulose, 81.
Starch paste, 81.
Stasis of blood in heart, 207.
Static activity of cerebellum, 611.
Static refraction in the eye, 519.
Steapsin, gastric, 250.
  in pancreatic juice, 253.
Stearic acid, 79, 701.
Stearin, 79.
Stentor, 43.
Stereoscope, Brewster's, 558, Fig. 251.
Stereoscopic vision, 558.
Sterkobilin, 295, 383.
Sterno-cleido-mastoid muscle, 316.
Sthenic activity of cerebellum, 611.
Stimulation, assimilation and, 62.
  by heat, 58, 59.
  by light, 56, 57.
  chemical, 52.
  electrical, 59, 60, 418.
  general laws of, 420.
  mechanical, 56.
  of muscle and nerve, 414.
Stimuli, in general, 50.
  of muscles and nerves, 410.
  of nerve cells, 569.
  rapidly repeated, 428.
  summation of, 572.
Stimulus, effect of, on performance of muscle, 435.
  effective, from minimum onward, 51.
  qualitative relations of, to sensations, 451.
  quantitative relations of, to sensations, 455.
  threshold value of, 455.
Stomach, absorption in, 303.
  antiseptic function of, 292.
  digestion in, 291.
  evacuation of, 285.
  innervation of musculature of, 284, Fig. 114.
  movements of, 283.
  principles as to digestibility in, 293.
  protective function of, 294.
  why not digest itself? 269.
Stomach fistula, see *Gastric fistula.*
Stomach glands, see *Gastric glands.*
Storage of carbohydrates, 124.
  of fat, 129.
  of phosphorus, 132.
  of proteid, 120; see *Retention of proteid.*
Strabism, muscular in the eye, 555.
Streamings of protoplasm, 42.
Stretching movements, influence of, on blood-flow, 225.
Stroma of red corpuscles, 150.
Stromuhr, 209, Fig. 80.
Strychnia, effect of, on nervous system, 570, 574.
Sublingual glands, 257; see also *Salivary glands.*
Sublingual saliva, 245.
Submaxillary glands, 257; see also *Salivary glands.*
Submaxillary saliva, 245.
Substance, living, constitution of, 20; see also *Protoplasm.*
  definition of, 15.
  relative stability of, 135, 137.
Substitution of foodstuffs, 93.
  of functions in the optic thalamus, 617.
  of tracts in the cord, 597.
Succinic acid, 297.
Sucking, 279.
Suction in heart, 177, 225.
  in mouth, 279; see also *Sucking.*
  in thoracic cavity, 176, 225, 310.
    diastole of heart and, 176.
    effect of, on blood pressure, 229, 230.
    effect of, on flow of lymph, 349.
  in veins, 225.
Sugar in blood, 155, 374.
  in muscles, 413.
  in urine, 127, 128, 362, 363, 374, 375, 384; see also *Diabetes.*
  origin of, 23.
  product of decomposition, 373, 374.
  production of, in liver, 374.
  storing of, as fat or glycogen, 374.
Sulphates, 373.
  ethereal, 373, 383.
Sulphocyanic acid, 373.
Sulphocyanide of potassium in saliva, 245.
Sulphur, acid, 373.
  elimination of, 373.
  in bile, 254.
  in proteid, 69.
  in urine, 383, 384.
  neutral, 373.
Sulphureted hydrogen, 295.
Summation as property of protoplasm, 51.
Summation in central nervous system, 572.
  in muscles and nerves, 429.
Surviving organs, 6.
Swallowing, 279.
  innervation of, 281.
  sounds of, 282.
Swallowing reflex, 280.
Sweat, collection of, in metabolism experiments, 85.
  composition and properties of, 395.
  excretory process of, 396.
  nitrogen in, 89.
  part played by, in heat regulation, 403.
  quantity of, excreted, 396, 408.
Sweat centers, 396, 588.
Sweat fibers, connections of, 582, 688.
Sweat glands, 395.
  innervation of, 396.
Sweet taste, 484.

Symbiosis, 22.
Sympathetic fibers, 686.
  afferent, 689.
  connection of, with peripheral ganglion cells, 582, 686, Fig. 301.
  course of, 687.
  postganglionic, 687.
  preganglionic, 686.
  regeneration of, 689.
Sympathetic ganglia, 582.
  connections of, 686, Fig. 301.
  reflexes through, 583.
Sympathetic nerves, 685.
  accelerator, of heart, 191, 688.
  as vasomotor nerves, 231, 234, 685, 688.
  of intestine, 288.
  of pancreas, 269.
  of receptaculum chyli, 349.
  of salivary glands, 258.
  of sebaceous glands, 394.
  of stomach, 284, Fig. 114.
  of thoracic duct, 349.
  of urinary bladder, 393.
Sympathetic vibration, 492; see also *Resonance*.
Syntheses in animals, 24; see also *Assimilation*.
  in plants, 23.
  of nonliving substances, 65.
  organic, 24.
Syntonin, 74.
System of organs defined, 30.
Systole, auricular, duration of, 176.
  definition of, 162.
  ventricular, duration of, 176.

Tabes dorsalis, 472.
Tactile corpuscles, 468.
Tactile sense, area of, in cortex, 651, 652.
Tail, vasomotor nerves for, 233.
Talbot's proposition, 539.
Tambour, receiving, 12, Fig. 10.
  recording, 11, Fig. 9.
Tartaric acid, 377.
Tartronic acid, 377.
Taste, cortical area for, 653.
  definition of, 451.
  effect of cocaine, eucaine, etc., on, 485.
  qualities of, 484, 485.
  sense of, 483.
Taste buds, 483.
Taste nerves, 484.
  reaction time to, 674.
Taste zone on tongue, 483, Fig. 190.
Taurin, 253, 373.
Taurocholic acid, 253.
Tears, layer of, on cornea, 508.
Tecto-spinal tract in the cord, 593.
Telencephalon or endbrain, 600, 601; see also *Cerebrum*.
Temperature, action of, on heart, 184, Fig. 66.
  effect of, on elimination of CO_2 and water vapor, 397, 403.
  influence of, on elementary organisms, 28.
    on metabolism, 114.
  of birds, 398.
  of cold-blooded animals, 46.
  of human body, 398, 399.
    after death, 401, Fig. 149.
    cause of variations in, 399.
    importance of clothes in preserving, 405.
    importance of thyroid for, 361.
    in fasting, 95.
    mode of recording, 398.
    normal compared with CO_2 excretion, 400, Fig. 148.
    normal diurnal variations of, 399, Fig. 147.
    normal for man, 398.
    regulation of, 406.
    supranormal, 401.
  of mammals, 398.
    constancy of, 401.
Temperature nerves, 461.
Temperature sensations, 458.
Temperature sense, area for, in cortex, 652.
  tract for, in cord, 597.
Temperature spots or points on the skin, 459, Fig. 182.
  topographical distribution of, 460, Fig. 183.
Temporal convolutions, 639, Fig. 289; 653, 655.
Tendon reflexes, 587.
Tension of gas in liquid, method of, 335.
Tension of gas in blood, method of, 341.
Tension of muscle, 414, 437.
Tension, osmotic, see *Osmotic pressure*.
Tensor tympani muscle, 497.
Terminal myelogenetic regions of cortex, 667.
Testes, 692.
  extirpation of, 357, 692.
  internal secretion of, 357.
Testicular extract, 357.
Tetanus, 429, Fig. 166; 430, Fig. 167; 433.
  explanation of, 430.
  number of stimuli necessary for, 429.
  of red and white muscles, 430, Fig. 167.
  Ritter's, 421.
  secondary, 433.
  work of muscles in, 439.
  Wundt's, 421.
Tetra-oxyamino-caproic acid, 374.
Thalamencephalon, 600.
Thalassicola nucleata, 18, Fig. 15.
  mode of movement of, 45.
Theca folliculi, 695.
Thermotaxis, 59.
Thigmotaxis, 56.
  of spermatozoa, 56, 697.
Thigmotropism, 64.

Thioalbumose, 249.
Thio-monamino acid, 70.
Thio-monamino-propionic acid, 70.
Thoracic cavity, 314.
  importance of suction of, for filling heart, 177.
  suction of, 176.
Thoracic duct, muscles and nerves of, 349.
Thoracic type of respiration, 317, 318, Fig. 126.
"Threshold difference," 456.
Threshold value of stimulus, 455.
Thrombin, 158.
Thrombogen, 158.
Thymin, 76.
Thyroid cartilage, 502.
Thyroid extract, 359.
  effects of treatment with, 359, Fig. 137; 360, Fig. 138.
Thyroid gland, 358.
  blood supply of, 240.
  chemistry of, 362.
  extirpation of, in dogs, 358.
    in man, 359.
    in monkey, 360.
  histology of, 361.
  innervation of, 361.
  internal secretion of, 358 seq.
  morphological changes in, 361.
  transplantation of, 359.
Timbre of sound, cause of, 491.
Time, determination of, in psycho-physical processes, 673.
Time recorders, 10.
Time stimuli, 423.
Tissue proteid, 134.
Tone deafness, 665.
Tone, fundamental, 491.
  musical, 489.
  produced by muscle, 434.
Tones, combination of, 501.
Tongue, action of, in swallowing, 279.
  taste nerves of, 484, Fig. 191.
  vasomotor nerves of, 235.
Tonic activity of cerebellum, 611.
Tonic excitation, state of, 581.
Tonus, cause of, 581.
  definition of, 581.
  demonstration of, in cross-striated muscles, 581.
  inhibition of, by stimulation of cortex, 636, 640.
  of blood vessels, 232.
Torpedo, 49, Fig. 30.
Total metabolism, after ingestion of carbohydrates, 106.
  after ingestion of fat, 104.
  after ingestion of proteid, 102.
  in fasting, 96.
  in growing children, 118.
  influence of work of digestion on, 107.
Touch, definition of, 451.
  end organs of, 468.
  sensations of, 461.
Touch reflex, 660.
Toxins, 40.
  in blood, 156.
Trachea, 502.
Tracts in spinal cord, 563 seq.
Transfusion, 207.
Transmission of stimulus, rate of, in muscle, 417.
    in nerves, 417.
    in spinal cord, 589.
Transudation, 207.
Treppe, 441.
Trichromatic color system, 545, 546.
Tricuspid valve, 165.
Trigeminal or trifacial nerve, 680.
  as nerve of smell, 488.
  as nerve of taste, 484.
  influence of, on respiration, 330.
Triglycerides, 79, 701.
Trioxypurin, 382.
Trochlear nerve, 680.
  nucleus of, 614.
Trophic centers in spinal ganglia, 568.
Trophic effect, definition of, 50.
Trophic influence of nerve cells, 569.
Trophic influence through motor nerves, 63.
Trophic nerves, 569.
Trophoblasts, 22.
Trypsin, 252.
  spleen and, 368.
Tryptophan, 71, 72, 109, 249.
Tuber cinereum, 600.
Tuning fork as time recorder, 10.
Turgor, 33.
Turtle, extirpation of cerebrum in, 621.
'Tweenbrain, or diencephalon, 600, 601, 617.
  importance of, in birds, 624.
    in bony fish, 619.
    in dogfish, 620.
    in frog, 620.
    in lizard, 621.
    in rabbit, 625.
    in turtle, 621.
Tympanic cavity, 495, Fig. 197; 497.
Tympanics membrane, 494, Fig. 196; 495, 496.
Tyrosin, 71, 72, 249, 255, 378, 384.

Ultra-red rays, 536.
Ultra-violet rays, 536.
  stimulating effect of, 57.
Unicellular organisms, 2, 15.
Uracil, 76.
Uræmia, 368.
Uræmic poisoning, 367.
Urates, 382.
Urea, amount of, in urine, 381.

Urea, amount of, in various organs, 382.
  as product of metabolism, 89.
  crystals, 382, Fig. 139.
  elimination of, in fasting, 101, Fig. 43.
  in blood, 155, 389.
  in sweat, 395.
  sources of, 370, 373.
  where formed, 370 seq.
Ureters, 391.
  muscular contractions of, 391.
Urethra, 392.
Uric acid, amount of, in urine, 382.
  composition of, 382.
  crystals, 382, Fig. 140; 383, Fig. 141.
  fate of, in mammals, 373.
  in blood, 155.
  microscopic detection of, in kidney, 388.
  production of, in birds, 371.
  properties of, 382.
  seat of destruction of, 373.
  sources of, 372.
Urinary bladder, 391.
  centers for control of, 393.
  innervation of, 392, Fig. 145; 393.
Urinary tubules, 385, Fig. 144.
Urine, amount of, excreted, 380.
  combustion heat value of, 93.
  composition of, 381.
  excretion of, 384.
    filtration theory, 387.
    secretion theory, 388.
  general properties of, 379.
  ratio of N:C in, 90.
  retention of, 393.
Urine indican, 379.
Urine mucoid, 380.
Urobilin, 295, 383.
Urochrome, 383.
Urotoxy, 381.
Uterus, 696.
  contractions of, 698, Fig. 302; 699, Fig. 303.
  growth of, in pregnancy, 698.
  innervation of, 700.
  menstrual changes in, 696.
  movements of, induced in various ways, 700.
  pressure curve in, in parturition, 699, Fig. 303.
Utilization of foodstuffs, 138.
  of energy, 139.
  of mixed diet, 139.
Utriculus of internal ear, 473.

Vacuoles, contractile, 22.
  in plant cells, 21.
Vagina, innervation of, 700.
Vagus nerve, 681.
  components of, 681.
  influence of, on blood pressure, 204 seq.
    on heart, 188, 190.
    on intestinal movements, 289.
Vagus nerve, influence of, on movements of stomach, 284, Fig. 114.
    on respiration, 327.
      explanation of, 329.
    on secretion of pancreas, 269.
      of stomach, 263.
Vagus pneumonia, 569.
Valves, atrio-ventricular, 165.
    closure of, 166, Fig. 54.
  semilunar, 166, 167, 171.
  venous, 225.
Vampyrella spirogyræ, 37, Fig. 23.
Vasa deferentia, 693, 694.
Vascular tonus, 232.
  adrenal bodies and, 366.
Vasoconstrictor nerves, 231, 596, 681, 685.
  connection of, with ganglion cells, 582.
Vasodilator nerves, 234, 681, 685.
Vasomotor centers, 237.
  influence of, on distribution of blood, 239.
  resistance of, to asphyxiation, 573, Fig. 257.
Vasomotor nerves, 231, 234, 688.
Vasomotor reflexes, 235.
Vegetable diet, 145.
Vegetable starches, 81.
Vegetarianism, 145.
Vegetative functions, conducting pathways for, 596.
  influence of cortex on, 649.
    spinal cord on, 587.
Veins, blood flow in, 223.
    influence of position of body on, 225, 226, Figs. 93, 94; 227.
  blood pressure in, 223.
  cubic distention of, 223, Fig. 92.
  innervation of, 233.
  valves of, 225.
Veins of Thebesius, 180, 181.
Velocity of blood in arteries, 210, Fig. 82.
  in capillaries, 221.
  in veins, 224.
Velocity of current in tubes, 198, 199.
Velocity of nerve impulse, 417, Fig. 155.
Velocity of pulse wave, 215.
Venæ cavæ, 161, 162.
Venomotor nerves, 233.
Venous blood, percentage of gases in, 339.
  tension of gases in, 341.
Venous ostia, 185.
Venous sinus, automaticity of, 183.
Venous valves, 225.
Ventilation of the lungs, 319.
Ventricles, 161.
  maximum pressure in, 170.
  negative pressure in, 177.
  structure of, 163.
  work of, 178.
Ventricular cavities, casts of, in rigor, 164, Fig. 53.

Ventrolateral cerebellar tract, 593.
Veratrin, effect of, on muscular contraction, 437, Fig. 175.
Vermis of cerebellum, 607.
  function of, 609.
Vertigo, an effect of cerebellar lesions, 608.
Vesical plexus, 392, Fig. 145; 393.
Vesicular glands, 691.
Vesicular noise, 322.
Vestibular nerve, 480, 681.
Vestibulo-spinal tract in cord, 593, 595.
Vibration frequency of tone, 489.
Vibration limits for organ of hearing, 490.
Vicia Faba, root tubercles of, 23, Fig. 18.
Vision, 508; see also *Eye*.
  binocular, 551, 552, Fig. 242; 555.
  direct and indirect, 514.
  limits of, 517, 518.
  line of, 518.
  stereoscopic, 558.
Visual angle, 518, Fig. 214; 556, 557.
  importance of, for perception of depth, 556.
Visual area for exact vision, 657.
Visual area of cortex, 655, 663.
Visual axis, 525; see also *Optical axis*.
Visual conducting pathways, 657.
Visual purple, 537, 541.
Visual sensations, as effected by eye movements, 552.
  elaboration of, 660.
  projection of, to external world, 552.
Visual substances, 546.
Vital capacity of the lungs, 320.
Vitalism, theory of, 2.
Vitellin, 75.
Vitellinic acid, 76.
Vitreous body, 508, 509.
  entoptic phenomena in, 521.
  refractive index of, 509.
Vocal cords, 502.
  movements of, in respiration, 312; 504, Fig. 202.
    in vocalization, 503, Figs. 200, 201; 505.
Voice, 502.
  change of, 692.
  pitch of, determination of, 505.
  production of, 504.
  registers of, 504.
Voit's theory of proteid metabolism, 134.
Volta's discovery, 47.
Volume, breath, 319.
  pulse, 204.
Voluntary muscular contractions, 430.
Vomiting, 286.
Vorticella, 44, Fig. 28.
  contraction in, independent of NaCl, 25.
  motility of, 43.
Vowels, how produced, 505, Fig. 204; 506, Fig. 205.

Wagner's hammer, 421, Fig. 159.
Wallerian degeneration, 567.
Warm-blooded animals, 46, 398, 405, 406, 441.
  reaction of, to external temperature, 114.
Water, absorption of, 302.
  a constituent of living substance, 20.
  determination of, in metabolism experiments, 85 seq.
  elimination of, through expired air, 89, 342, 404.
    through kidneys, 89, 379.
    through skin, 89, 397, 404.
  requirement in fasting, 95.
Wave lengths of visible light rays, 536.
Weber's theory of the pulse, 213, Fig. 85.
Weber's law, 456.
Weight, estimation of, 469, 470.
  growth in, of human body, 707 seq.
  sensation of, 471.
White matter of spinal cord, 562.
White rami communicantes, 686, 689.
Will, influence of, as stimulus, 570.
  power of, over pain, 466.
Window, oval, of ear, 496.
  round, of ear, 497.
Witch's milk, 704.
Word blindness, 663, 669.
Word deafness, 664.
Work, assimilation and, 63; see also *Muscular work*.
  external, and total energy, 113.
  of heart, 178.
Worker, moderate, nutritive requirements for, 142.
Woman's milk, 701.
Women, nutritive requirements for, 143.
Wundt's tetanus, 421.

X rays, 58.
Xanthin, 76, 252, 413.
Xanthin bases, 76, 434.
Xantho-proteïc reaction, 72.

Yellow as brightest light, 541.
Yellow-blue blindness, 547.
Yellow spot, 517.
Yolk spherules of ovum, 695.
Young, metabolism in the, 118.
  nutrition of the, 143.
Young-Helmholtz' theory of color vision, 544.
Youth, age of, 706.

Zona pellucida, 16, 695.
Zonule of Zinn, 533, Fig. 228.
Zymase, 40.
Zymogens, 38, 244.
  activation of, 38, 252.

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